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Archives of Neurology and Psychiatry

VOLUME 22 OCTOBER, 1929 NUMBER 4

ENCEPHALOMYELITIS DISSEMINATA *

WILLIAM G. SPILLER, M.D.
Professor of Neurology in the University of Pennsylvania
PHILADELPHIA

Though long recognized, encephalomyelitis disseminata has attracted much attention from foreign neurologists during the past few years, but seems to have been largely ignored by American neurologists, although its relation to measles has been studied by Neal and Appelbaum, Musser and Hauser and Ford.

It has been thought by some that cases of encephalomyelitis disseminata have become more numerous since the appearance of epidemic encephalitis. The relation between encephalomyelitis disseminata, acute multiple sclerosis, encephalomyelitis of infectious diseases (exanthems), especially of variola and preventive variola vaccination, and neuromyélite optique aiguë has become important and difficult to determine.

Two cases of encephalomyelitis disseminata are reported, one with recovery and one with necropsy.

REPORT OF CASES

CASE 1.—*History.*—C. B., a man, aged 40, was admitted to my service in the University Hospital on May 6, 1926, and was discharged on June 10, 1926. The patient was in good health, doing his daily work, until thirteen days previous to admission, when on rising in the morning he noticed that both lower limbs were "asleep," i. e., they felt numb and tingling; they were equally weak and it was difficult for him to move them. He went to work as usual, but worked only half a day. He had not been drowsy; he had no confused ideas, convulsions, twitchings, headache, pains or vomiting. The next morning, the lower limbs were weaker, and he noticed for the first time that he had double vision and some difficulty in moving the left side of the face; the diplopia lasted for four days and then disappeared. The facial weakness lasted until May 5. Neither was severe. One week previous to entrance to the hospital, he became slightly hoarse and noticed that his speech was a little "thick," as though there were a lump in his throat. He had no difficulty in finding the words he wished to speak, i. e., he had no aphasia. During the next few days these symptoms had greatly improved. About a week before admission, he noticed that his hands felt numb as though they were "asleep," and they likewise became slightly weak. At the time when speech was affected the lower limbs became so weak that he was compelled to go

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* From the Department of Neurology and the D. J. McCarthy Foundation in Neurology, of the University of Pennsylvania.

* Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 27, 1929.

to bed or sit in a chair because he could not stand. All the symptoms had improved except those of the hands and lower limbs, and these were becoming steadily worse. He had no disturbance of urination. Mentality was not affected. He could not stand nor walk.

Examination.—Both upper limbs showed dysmetria. Adiadokokinesis was slight in the upper limbs and these limbs presented a coarse tremor.

The pupils were round, regular and equal, and reacted promptly to light and in convergence. The margins of the disks were slightly hazed and hyperemic. He did not have extra-ocular muscular weakness or nystagmus, but did have slight weakness of the left side of the face when drawing up the corners of the mouth. The soft palate was paralyzed. The tongue showed some fibrillary tremors and a tendency to slight deviation to the right when protruded. No disturbance of sensation was found in the face. There was some difficulty in swallowing.

The muscles of the trunk were weak, and expansion of the chest was slight. The upper limbs were weak but much more powerful than the lower. The grasp of each hand was very weak. The biceps and triceps reflexes were lost on each side. Touch, pain, heat, cold, position and passive movement sensations were normal in the upper limbs, but vibration sensation may have been a little impaired in the hands. Stereognosis was normal.

Slight voluntary motor power was possible in all joints of the lower limbs, but the patient could barely lift his knees from the bed and could move the feet very slightly, even the toes. The patellar reflexes were entirely lost, even on reinforcement, as were the achilles reflexes. The Babinski reflex was without any movement of the toes on either side. Pain, touch, heat and cold sensations were entirely normal in the lower limbs. Vibratory sensation was lost in the lower limbs, except that occasionally it seemed to be recognized over the right patella. Sensation of position was lost in the toes and ankles, but not in the knees. The cremaster reflexes were distinct, and the abdominal reflexes were obtained.

The blood pressure was 130 systolic and 80 diastolic. The urine showed hyaline and epithelial casts. The Wassermann reaction of the spinal fluid was negative. The spinal fluid showed 1 cell to the cubic millimeter. No culture was obtained from the spinal fluid. There was a trace of globulin. On May 9, a Wassermann test of the blood gave: acetone, negative; cholesterin, delayed negative; icebox modification, strongly positive; Kolmer, 444——. The clinical picture suggested a Landry's paralysis. An examination of the feces gave negative results. Massive blood cultures were reported negative on May 26.

Course.—On May 13, I made a note that recovery of power in the limbs, especially the lower limbs, since admission had been extraordinary. He had good power of extension and flexion in the lower limbs, though the power was far from normal. The dynamometer registered 20 in the right hand and 15 in the left hand. The patient was able to use the trunk muscles to sit up. On May 21, it is recorded that the weakness of the left side of the face had disappeared, although the soft palate was still weak. Dynamometer tests with the right hand gave 70, and with the left hand, 50. No antisyphilitic treatment was given before May 22, when mercury was administered. The improvement, therefore, could not have been caused by this.

On May 16, a culture from the throat showed the predominating organism a streptococcus, forming enormously long chains; there were a few tetrad forms, probably *Micrococcus tetragenus;* it was negative for Klebs-Loeffler bacillus and *Streptothrix.*

When the patient left the hospital, on June 10, he was able to sign a paper, but showed tremor in writing. His general condition was good. A report received

from him on March 24, 1929, stated that he went to work on Aug. 1, 1926, and had been working since.

CASE 2.—*History.*—H. L., a man, aged 34, was admitted to my service in the University Hospital on November 20, and died on Nov. 22, 1924. He was in the hospital only two days. Death took place from acute bulbar palsy.

The illness began on Oct. 6, 1924, when, after returning from an automobile trip, the patient complained that his feet felt as though they were "asleep"; they were numb and tingled. On awakening the next morning, the tingling had reached the ankles. The numbness and tingling continued to ascend the limbs until the paresthesia had reached the level of the hips on October 10. The patient felt well in every other respect and continued his work. He could walk well even in the dark. During the night of October 11, he awoke with a sharp pain in the right side of the chest just below the clavicle. This became more severe. Two hypodermic injections were given to control the pain. During the next week he had three more similar attacks of pain, two of which were on the left side. Wassermann tests of the blood and roentgen examination of the chest and spinal column gave negative results. The patient remained in bed most of the week, from October 19 to 26. On October 22, the spinal fluid showed an increased cell count. The paresthesia in the lower limbs improved somewhat, but by November 10 he noticed slight paresthesia in the right hand and right side of the face, and he had a girdle sensation. He tired easily on walking. He vomited from November 11 to 17.

He had no fever at any time. On November 15, some hoarseness was noticed. This became more marked and the patient had great difficulty in speaking and swallowing. The mucus in the throat was excessive.

He did not have diplopia at any time. He had not been paralyzed in his limbs, but tired easily. The blood pressure was 130 systolic and 85 diastolic. The Wassermann reaction of the blood was negative.

Examination.—On admission he was confined to bed, breathed with some difficulty and mucus collected in the throat and was not easily expelled. Ability to swallow was greatly impaired. He spoke with great difficulty, and his voice was indistinct. He was mentally clear and cooperated fairly well in the examination. Hearing seemed slightly impaired. Speech was nasal. Corneal and conjunctival reflexes were absent on each side. The facial nerve was not affected. Pain sensation was distinctly impaired in the left side of the face, but tactile sensation was not impaired. He had right lateral nystagmus. The pupils reacted normally to light and in convergence. The soft palate was paralyzed on each side and fluid regurgitated through the nose. The tongue was not affected. The abdominal reflexes were absent. The dynamometer in the right hand registered 25, in the left, 105. The patient was left-handed. The biceps and triceps reflexes were barely perceptible. Pain and temperature sensations were greatly impaired in the left upper limb and left side of the trunk, but touch sensation was preserved. Adiadokokinesis and dysmetria were present on the right side. Stereognosis was impaired.

The power in the lower limbs seemed equal. The patellar reflex was normal on the left and increased on the right side. The Babinski sign was not present. Sensation of position was impaired in the toes of the right foot. Impairment of pain and temperature sensations was found in the entire left lower limb, but touch sensation was normal.

Course.—On November 21, notes were made that the pulse rate had been as low as 52, and that the patient was too weak for examination. The temperature was rising, and he died the following day.

Postmortem Examination.—The cervical cord, except the uppermost part, was not obtained. There was an area of myelitis about the first or second thoracic

segment. The lesion was central, it contained vessels with intense lymphocytic infiltration about them, recent hemorrhages and lacelike structure (status spongiosus) at the periphery of the lesion. The affected area extended nearly to the periphery of the cord in the posterior columns, and this may explain the paresthesia beginning in the feet. The lateral columns were much affected near the central gray matter, but their peripheral portions seemed nearly, if not fully, normal. Numerous monstrous or giant cells (gemästete glia cells) were found, especially at the border of the degenerated area; they were fiber-forming astrocytes. There was no unusual vascularization of the cord, and the vessels did not show distinctly thickened walls in the degenerated area, or distinct changes in their endothelial cells. A few gitter cells were detected by the Globus modification of the Cajal stain, which showed well the giant astrocytes. The infiltration in the lesion appeared to be of lymphocytic cells, and was intense about some of

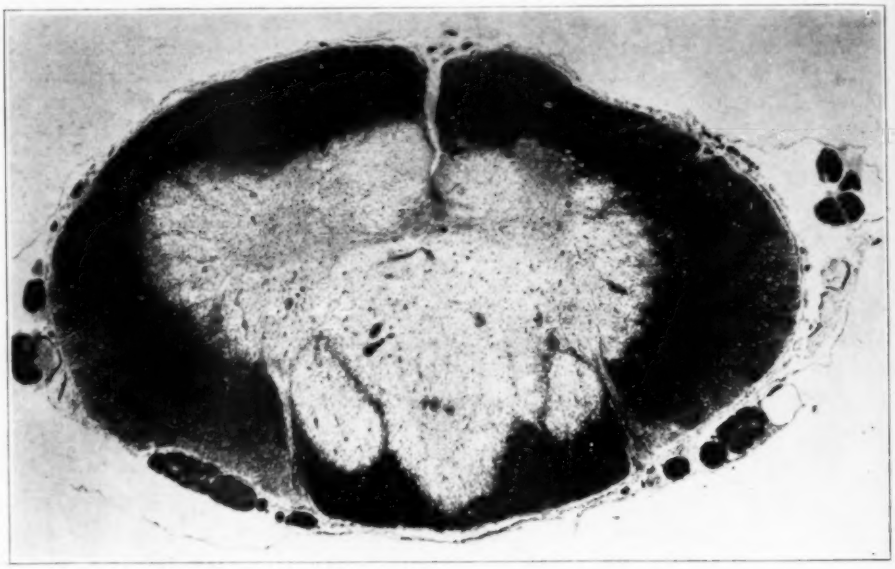

Fig. 1 (case 2).—Section from the upper thoracic cord, showing degenerated area.

the vessels. Scattered small hemorrhages were numerous in the lesion. The pia did not show distinct cellular infiltration. Fat stains were not made, as the affected area was limited in the portion of cord obtained, and there was not sufficient material. The nerve cells of the anterior horns in the lumbar region appeared normal. The demyelination was not perivascular.

A similar area was found in the left lateral portion of the medulla oblongata, in the region of the restiform body. This area did not extend through many sections. It corresponded in location to the degeneration produced by occlusion of the posterior inferior cerebellar artery. Severe lesions were not found in the pons, though there was slight lymphocytic infiltration about a vessel here and there. Recent severe hemorrhages were found in the substantia nigra on each side.

Dr. Herbert Fox reported on the examination of tissue sent to him as follows:

"Careful staining and study for bacteria in the pons tissue that you sent us failed to reveal them. Especial attention was given to small areas of focal

necrosis of the fibers, and to the occasional areas of round cell infiltration in the vicinity of blood vessels.

"The discovery of *Micrococcus tetragenus* in the arachnoid and the ventricular fluid is perfectly credible. I have seen a case of meningitis from the spinal fluid of which this organism was cultivated in pure culture; I have also seen the organism recovered in a blood culture, in a case of septicemia during the puerperium. The organism is almost confined to the respiratory tract, although I have recovered it from the urethra. It has been found in human milk. I know of no studies that would show the possibility of this organism being a postmortem invader of tissue so completely that it would penetrate the brain. It is a local

Fig. 2 (case 2).—Degenerated area in the left side of the medulla oblongata.

colonizer. It is, of course, nonmotile; its power of infiltration in the lung and bronchi would not seem to be great. I am inclined to look at this discovery therefore as indicative of the presence of the organism before death.

"*Micrococcus tetragenus* is best known in subacute and chronic bronchitis, bronchiectasis and pulmonary abscess, in all of which it is probably secondary to some other infecting agent. When it spreads from the respiratory tract it would seem to do so mechanically, or by the ulceration of the process in which it is involved into a blood vessel.

"It is a common secondary in tuberculous lesions and is credited with having some penetrating power in the vicinity of these lesions. It has been found in isolated abscesses. One authority describes it as frequently present in the normal vagina."

COMMENT

Summary of Case 1.—A man, aged 40, previously healthy, found on arising one morning that he had numbness and weakness in both lower limbs. He worked half a day. The following morning the lower limbs were weaker and he had diplopia and weakness of the left side of the face. The diplopia lasted only four days. The facial weakness lasted about eleven days. Hoarseness and thickness of speech developed. About a week after the onset the hands became numb and slightly weak. The weakness of the lower limbs increased and standing became impossible.

Fig. 3 (case 2).—Degenerated area in the left side of the medulla oblongata.

When he came under my observation the margins of the disks were slightly hazed, there was slight weakness of the left side of the face, the soft palate was paralyzed, the tongue showed fibrillary tremors and deviated slightly to the right and swallowing was a little difficult. The lower limbs were almost paralyzed, and the patellar and achilles reflexes were almost lost. No movement of the toes was obtainable in the Babinski reflex. Vibratory sensation was lost in the lower limbs and sensation of position was lost in the toes and ankles. The muscles of the trunk and upper limbs were weak, but more powerful than those of the lower limbs. The biceps and triceps reflexes were lost. A week

after admission the patient had regained much of the power in all his limbs and gradually recovered entirely.

Case 1 suggests poliomyelitis, but grave objective disturbances of sensation do not occur in a typical case of this disease, although they have been reported in a few cases. Pain, touch, heat and cold sensations were entirely normal in the lower limbs, but vibratory sensation was lost in the lower limbs, except that occasionally it seemed to be recognized over the right patella. Sensation of position was lost in the toes and ankles, but not in the knees. Vibratory sensation seemed to be

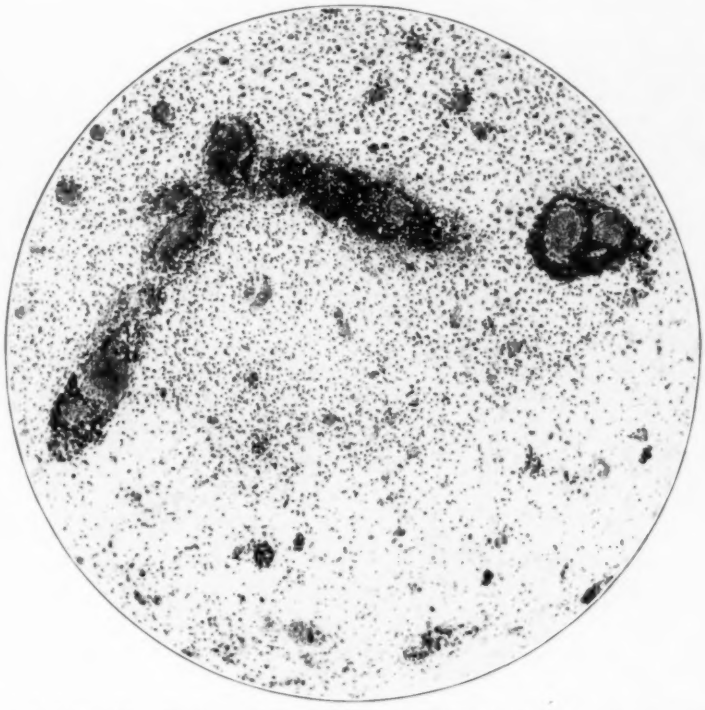

Fig. 4 (case 2).—Perivascular cellular infiltration in the degenerated area of the cord (see fig. 1).

somewhat impaired in the hands. For these reasons I have classed the case under the diagnosis of encephalomyelitis disseminata.

Summary of Case 2.—A man, aged 34, previously healthy, on Oct. 6, 1924, complained of numbness in the feet; in four days this numbness had ascended to the hips. He continued working and could walk well. During the night of October 11, he had severe pain in the upper part of the right side of the chest and later had pain at the same level in the left side of the chest. The spinal fluid showed an increase of cells. By November 10, paresthesia was felt in the right hand and

right side of the face. Walking caused fatigue. There was no fever. Hoarseness and great difficulty in speaking and swallowing developed. There was no diplopia.

The patient came under my observation on Nov. 20, 1924. Speech was nasal and the soft palate was paralyzed bilaterally. Pain but not tactile sensation was impaired in the left side of the face. Lateral nystagmus was present on looking to the right. The abdominal reflexes were absent. Pain and temperature sensations, but not tactile sensation, were greatly impaired in the left upper and lower limbs and left side of

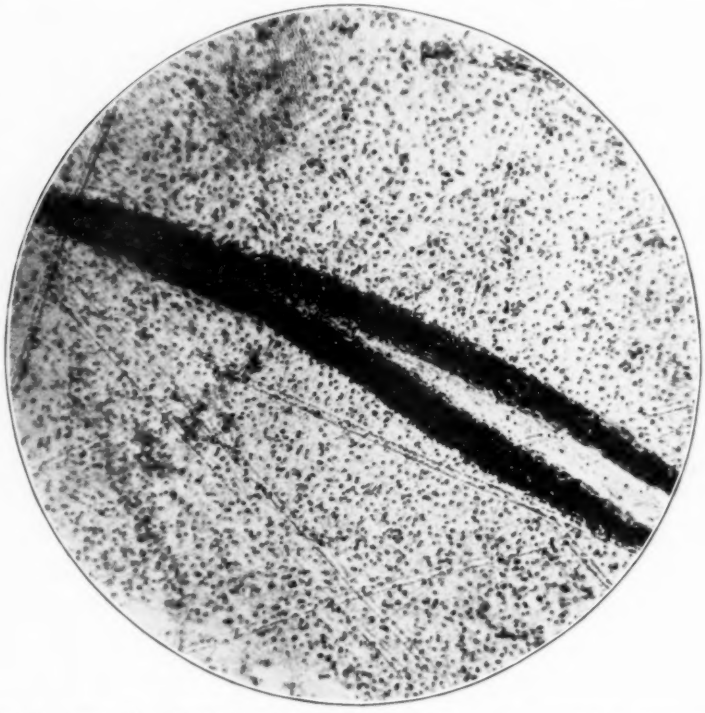

Fig. 5 (case 2).—Perivascular infiltration in the degenerated area of the medulla oblongata.

the trunk. The limbs were not paralyzed but tired easily on exertion. The patient was too ill for more careful examination and died two days after admission.

Case 2 is included also under the designation of encephalomyelitis disseminata. It was one of ascending paresthesia, but not of ascending motor paralysis. The lesion in the posterior columns may possibly explain the paresthesia, and the most peripheral fibers in the posterior columns may have been first affected. It is interesting to note that the ascending paresthesia must have been caused by a lesion of the

first or second thoracic segment, as the cord below this level was intact in many sections examined. The attacks of intense pain on each side of the chest just below the clavicle must have been produced by involvement of the upper posterior roots in the lesion of the posterior columns.

This case presented two well defined foci of altered tissue, in which demyelination with hemorrhages and perivascular lymphocytic infiltration occurred. It would seem that these observations justify the designation employed.

There is doubt as to what is the pathology of encephalomyelitis disseminata. Is it an inflammatory or a degenerative process? Hassin has stated, and Winkelman has supported him in this statement, that it may be impossible to determine the character of the cells in perivascular infiltration except by differential stains. A gitter cell containing little fat may resemble a lymphocyte so closely that the distinction may be possible only by the use of a fat stain to determine the existence of the gitter cell. I do not find this distinction mentioned in the literature, and it complicates the pathologic diagnosis. Penfield has made the interesting suggestion that a gitter cell after discharging its fatty degenerated material in the perivascular space may reenter the degenerated area for further phagocytosis. There is nothing unreasonable in this.

There are those who hold that encephalomyelitis disseminata is not acute multiple sclerosis; others do not make a sharp distinction. In my fatal case the numerous cells about the vessels appeared to be identical with lymphocytes, but I found in the lesion in the medulla oblongata that some of the cells resemble gitter cells. It is unfortunate that a fat stain could not be employed. The demyelinated areas in the spinal cord and medulla oblongata in their general appearance resembled plaques of multiple sclerosis. The demyelinated areas in acute multiple sclerosis contain chiefly microglia (gitter cells). It is possible that if fat-bearing cells have much to do with making a process one of acute multiple sclerosis the diagnosis of this disease will be made more frequently. One expects gitter cells to be found whenever the degeneration in the central nervous system is acute and with demyelination; whether they will appear in the form long recognized as the fatty granular cell or in that resembling a lymphocyte so closely that it can be determined only by a differential stain will depend largely on the duration of the lesion. Bouman and Bok asserted that the fatty granular cell does not occur in epidemic encephalitis.

I have reexamined the sections from the case of acute poliomyelitis studied by me and reported with Sherman [1] in 1900, also the sections from two other cases of acute poliomyelitis. In all, the cellular infiltra-

1. Sherman and Spiller: Phila. M. J., March 31, 1900.

tion was intense and seemed to be chiefly of lymphocytic type, with cells of the type called polyblasts by Wickman.[2] The peculiar features of poliomyelitis depend chiefly on the selective affinity of the disease for the anterior horns, although these are not the only structures attacked. Some of the infiltrating cells can be seen to possess a cell body. Very little is known about the organisms of the group of cases under consideration in this paper. Poliomyelitis causes areas of demyelination in the anterior horns of the spinal cord though not in the white matter.

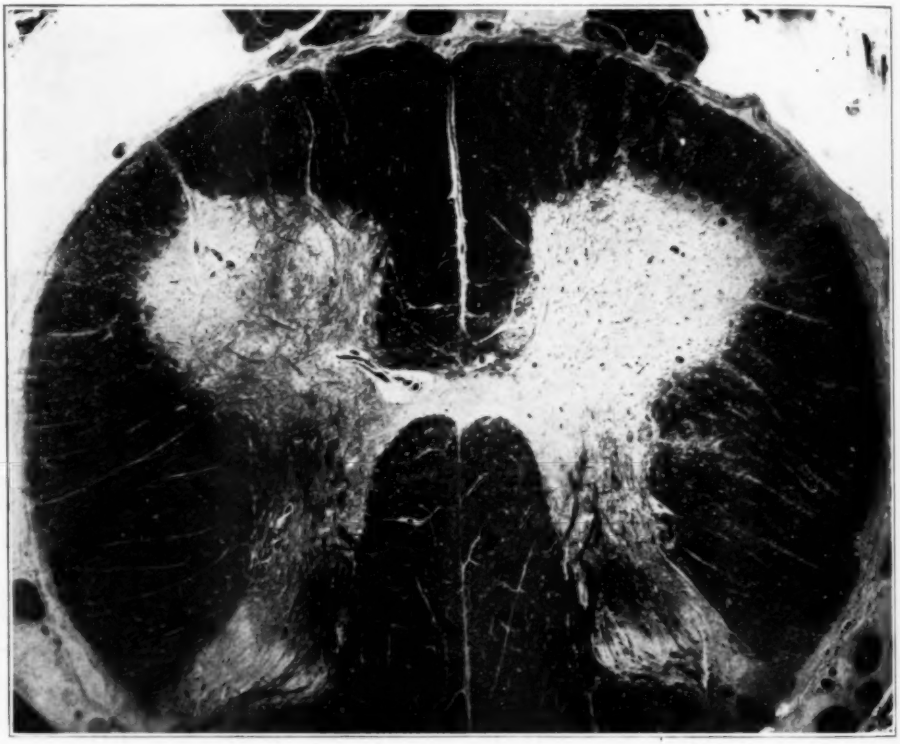

Fig. 6.—Degenerated anterior horns of the cord in variola. (The observations at this level resemble those of anterior poliomyelitis.)

Wickman believed that he had solved the much disputed character of the infiltrating cells in poliomyelitis. He said that the principal cells are not leukocytes, or proliferated connective tissue elements, nor are they simply lymphocytes. They represent a further stage in the development of the lymphocyte and are what Maximov has described as polyblasts. These are derived from lymphocytes, in which the nucleus stains lightly, a dainty network distinctly appears in the cell

2. Wickman: Acute Poliomyelitis, translated by Maloney.

and the protoplasm has increased. These cells later develop into types —as is evident from three or four of the larger forms in the figure given—which have no resemblance to the mother cells, to which, however, numerous forms link them. The origin of these cells from lymphocytes may therefore be considered as proved. Spielmeyer criticized the limitation of the term polyblast by Wickman to this one type of cell.

In comparison with these cases the case of subacute multiple sclerosis reported by me [3] in 1919 is of much interest. This seems to have been the first case of this type with necropsy reported in this

Fig. 7.—Degenerated areas in the lateral column in variola, showing disseminated perivascular demyelination. (Same case as shown in figure 6. The observations at this level are unlike those of anterior poliomyelitis.)

country. The paper was read by title before the American Neurological Association in 1917.

In a man, aged 25, the symptoms began in February, 1915, with headache. In June, 1915, vision began to fail. In July, 1915, optic neuritis was observed. Weakness of the limbs developed gradually, with nystagmus, incoordination, vertigo, scanning speech, intention tremor and progressive impairment of gait, until walking finally became impossible and mentality was very feeble. Death occurred on Dec. 21, 1916.

3. Spiller, W. G.: Subacute Forms of Multiple Sclerosis, Arch. Neurol. & Psychiat. **1**:219 (Feb.) 1919.

The necropsy revealed practically nothing abnormal with the viscera. The areas of sclerosis were numerous and were found in every section taken from the spinal cord, but they were more pronounced in the cervical and lumbar regions than in the thoracic region. In some places these areas were fairly sharply defined from the normal tissue, but in many places the shading off into normal tissue was observed. Lacelike structure was found in some of the patches. The areas were infiltrated with numerous mononuclear cells, and these were especially numerous about the blood vessels within the cord and in some of the septums running into the cord. These cells were numerous in the pia of both the cord and the brain, and in some places formed dense masses. The large spider cells (Deiters' cells), so numerous in the foci within the cerebrum, were not found in the cord.

Fig. 8.—Extraordinary symmetry in degenerated areas of multiple sclerosis.

The alteration in the medulla oblongata was as intense as in the cord. The Marchi sections of the cord and brain showed intense recent degeneration, except in areas of long standing in the cord. The nerve cells of the anterior horns of the cervical and lumbar regions were well preserved even in sclerotic foci, as shown in the thionine stain, and did not show pigmentary degeneration, although occasionally a cell showing chromatolysis and swelling was found.

The optic chiasm, tracts and nerves were greatly degenerated and showed much infiltration with cells of mononuclear type. Some foci of degeneration were found in the cerebellum, as in the right dentate nucleus.

Sections from many parts of the cerebrum showed disappearance of medullary substance in the altered areas. The sharpness of definition of the degenerated from the normal tissue was possibly even more pronounced here than in the spinal cord. The nerve cells in the altered cortex were well preserved. The cerebral foci contained many large glia cells (Deiters' cells), mononuclear cells and fatty

granular cells, and these foci differed greatly from the foci in the spinal cord in that the former were almost entirely cellular.

The cells in the cerebral foci belonged chiefly to the microglia and were gitter cells. The Marchi stain showed the presence of fat in these cells. The cells described as Deiters' cells have been described in more recent work as monstrous, giant or gemästete glia cells. Some of these suggested that they were partially degenerated astrocytes. The peculiar feature of acute multiple sclerosis was the sharply defined areas of cellular growth consisting chiefly of gitter cells.

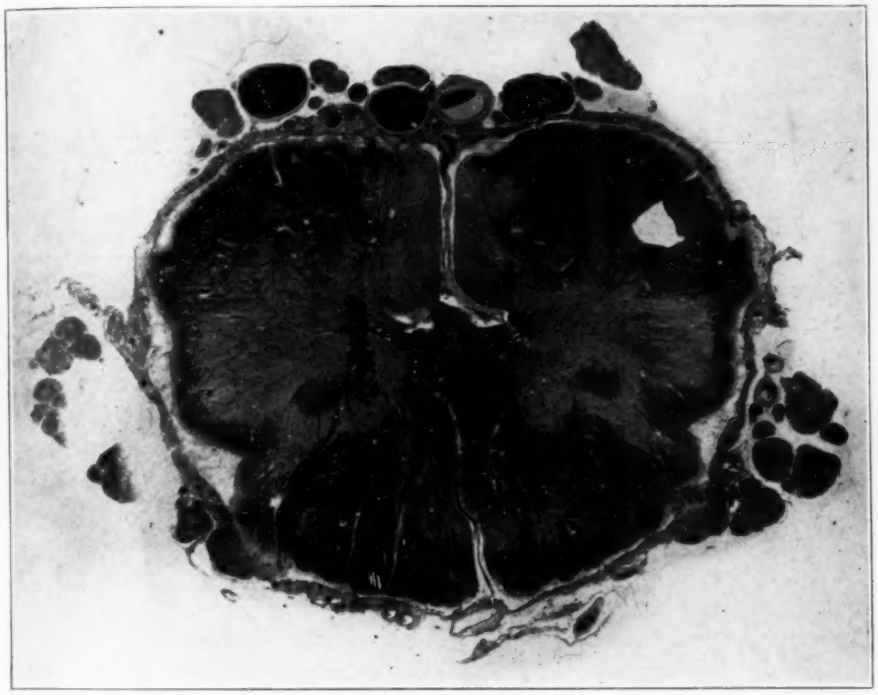

Fig. 9.—Extraordinary symmetry in degenerated areas of multiple sclerosis. (Same case as shown in figure 8. The symmetry of the degeneration was found throughout the spinal cord.)

I have had no experience with postvaccinal encephalomyelitis, but in 1903 I reported a case of variola with perivascular demyelination.[4]

The patient was 38 years of age. Paraplegia occurred during variola on the eighth day of the eruption. Death terminated the illness on the thirty-sixth day of the disease.

About the midthoracic region the gray matter of the anterior horns was chiefly affected, and portions of it stained faintly by the Weigert hematoxylin method, but in this region the white matter was considerably implicated. In the lumbar region the anterior horns showed demyelination, but the white matter was scarcely

4. Spiller, W. G.: Brain **26**:424, 1903.

implicated. The midthoracic region presented numerous patches of demyelination about vessels in the lateral columns, especially of one side of the cord, and to some extent in the posterior columns. Gitter cells stained by the Marchi method were found in the faintly staining areas and about the blood vessels. The nerve cells of the anterior horns presented more or less chromatolysis, displacement of the nuclei and loss of dendritic processes, but the alteration of nerve cells was not intense. The perivascular lymphocytic infiltration was slight.

The changes observed in the lateral columns are like those reported by Turnbull, Bouman and Bok [5] and others in postvaccinal encephalomyelitis. The foci in Bouman and Bok's case contained few, if any, hematogenous cells.

The patient I reported exhibited one fair and two poor vaccine scars from vaccination in childhood. Evidently he had not been vaccinated recently, although no statement is made regarding this. These observations are unlike those reported by Eichhorst.[6]

In Eichhorst's case, the observations of variola myelitis were likened by him to those of acute poliomyelitis. His patient died a few days after the onset of the disease. Numerous disseminated inflammatory foci were found throughout the spinal cord. These foci consisted of mononuclear round cells which were especially numerous near the blood vessels, and contained hemorrhages. Nothing is said of demyelination. This is the only case of involvement of the spinal cord in variola in man to which Bouman and Bok referred; they spoke of it as not entirely satisfactory.

The chief interest in my case is the resemblance of the lesions to those of postvaccinal myelitis but this does not prove that the virus is the same in the two diseases.

McIntosh [7] examined the brain of a child in whom cerebral symptoms developed after a mild attack of smallpox. He found perivascular small cell infiltration, characterized by a slight infiltration of the vessel sheath, or a more diffuse, wide infiltration of the surrounding parenchyma, with well marked demyelination of the nerve fibers. The cellular infiltration was composed mainly of large cells with oval clear nuclei, together with a number of lymphocytes. Polymorphonuclears were uncommon, as were also plasma cells. The meninges were only slightly involved. The cord was not obtained. The lesions showed a striking similarity to those of postvaccinal encephalitis.

This author said that histologic and experimental research have shown that the lesions in the encephalomyelitis of vaccinia and smallpox are identical, characteristic and definitely distinct from those of poliomyelitis and epidemic encephalitis.

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5. Bouman and Bok: Ztschr. f. d. ges. Neurol. u. Psychiat. **111**:495, 1927.
6. Eichhorst: Deutsches Arch. f. klin. Med. **111**:1, 1913.
7. McIntosh, J.: Brit. M. J. **2**:334 (Aug. 25) 1928.

Epidemic encephalitis has been excluded by most writers from the group of cases considered in this paper, and the reasons given are the clinical manifestations in the typical case of this disease, and the selective action of the inflammation for the gray matter instead of the white matter, as occurs in multiple sclerosis, also the absence of plaques of demyelination in epidemic encephalitis. Such plaques undoubtedly do occur rarely. I reported finding a small one in a case of epidemic encephalitis at the meeting of the Association for Research in Nervous and Mental Disease (1920) devoted to a discussion of this disease, and still more pronounced plaques I reported in the case studied with Jones.[8]

I have seen the gray matter of the pons and medulla oblongata chiefly involved in acute multiple sclerosis, although the white matter of the spinal cord was severely affected. The value of the greater involvement of the gray matter of the midbrain in epidemic encephalitis as a distinguishing feature is, therefore, of questionable value.

Bouman and Bok emphasized that the lesion is widespread and diffuse, not focal, in epidemic encephalitis, and is most intense in the mesencephalon; the perivascular cells are lymphocytes and plasma cells or polymorphonuclear cells, forming a mantle about the vessels. The reaction of the glia is slight. The microglia and macroglia cells show moderate increase, but fatty granular cells do not form. Neuronophagia occurs mostly from oligodendritic glia cells, but also from hematogenous cells. When the white matter is invaded most of the medullary sheaths and axis cylinders remain intact.

In 1927, Redlich[9] described a large number of cases in which within a few weeks or even a few days symptoms of a severe disorder of the spinal cord or of the brain and spinal cord developed, and gave manifestations suggesting a transverse lesion of the cord, of Brown-Séquard paralysis or of diffuse lesions of the brain and spinal cord. The symptoms were grave, but in many cases recovery occurred, in some as rapidly as the onset. He thought at first of acute multiple sclerosis, and there was much in these cases to suggest this diagnosis, but symptoms of a transverse lesion of the cord or Brown-Séquard paralysis are exceptional in multiple sclerosis. In all the cases the optic nerve was unaffected, and yet symptoms of disturbance of the optic nerve are among the most diagnostic of multiple sclerosis. In a large proportion of cases of acute multiple sclerosis the termination is fatal, whereas in Redlich's cases rapid recovery occurred in the majority. He did not accept multiple sclerosis also because of the acute onset in persons previously healthy, the severity of the symptoms in the early stage,

8. Jones, I. H., and Spiller, W. G.: Brain **48**:334, 1925.

9. Redlich, E.: Monatschr. f. Psychiat. u. Neurol. **64**:152, 1927.

the absence of general cerebral symptoms and of psychic disturbances and the failure of distinct exacerbations.

For these reasons he preferred the diagnosis myelitis disseminata or encephalomyelitis disseminata, a term by no means new. He recognized that multiple sclerosis has been regarded as encephalomyelitis, but he preferred to regard these two as separate disorders although he acknowledged that the distinctions are not sharply drawn. He reported only one necropsy and the observations from this were unsatisfactory.

Most of Redlich's cases occurred within a comparatively short time. He could not assert that they represented a special form of infection. He considered epidemic encephalitis without accepting it, but preferred to group his cases with the encephalitis from infectious diseases: varicella, measles and variola vaccination.

The paper by Redlich at once created great interest, partly because of the unusually large number of cases he reported (more than eleven) and partly because of the large proportion of recoveries.

Pette [10] stated that he has observed that certain forms of encephalomyelitis have become more frequent since the close of the World War. The cases to which he referred are difficult to classify under well known disorders. He did not believe that these cases, which appear clinically as encephalitis, myelitis or more frequently encephalomyelitis, are to be regarded as presenting a new disease, but rather as one closely related to multiple sclerosis. He referred to similar cases reported by Ley and van Bogaert.

Pette believed that neither from the symptoms nor from the pathologic observations is it possible to separate clearly encephalomyelitis and multiple sclerosis, and he quoted numerous authors in support of this statement. He thought that multiple sclerosis can be considered when there is really sclerosis, i.e., a circumscribed overgrowth of fiber-forming glia. This demands a certain duration of the process; therefore, the diagnosis of multiple sclerosis can be made only when sufficient time has elapsed for sclerosis to form, and anatomically it may be impossible to separate disseminated encephalomyelitis from multiple sclerosis.

In his three cases, perivascular infiltration was of different intensity. He believed that the intensity of mesodermal reaction depends on the age of the process. The same is true for the meninges, but in his three cases the cells in the interior of the foci were chiefly microglia (gitter cells). He showed a close relationship pathologically between measles encephalitis, variola vaccine encephalitis and multiple sclerosis, but he stated that encephalomyelitis disseminata recently has been recognized by Redlich, Henneberg and Wohlwill as an independent disease. He considered the pathologic observations in some cases of poliomyelitis,

10. Pette, H.: Deutsche Ztschr. f. Nervenh. **105**:76 (Sept.) 1928.

at least in the acute stage, as having certain resemblances to those of encephalomyelitis disseminata. Siemerling and Raecke, as well as Fraenkel and Jacob, found a relationship between poliomyelitis and multiple sclerosis. This has to do with the fact that in all these disorders the primary affinity of the active agent is for the ectodermal tissue; the mesodermal is affected only secondarily. Levaditi employed the term "ectodermoses neurotropes" for these diseases.

In Pette's three cases the pallidum, the nucleus ruber, the substantia nigra and the corpora mammillaria were not implicated in the lesions, but in my case the substantia nigra showed numerous small hemorrhages on each side.

Bouman and Bok described the observations in acute multiple sclerosis as scattered foci, chiefly in the white matter, and somewhat more frequent in the spinal cord. Demyelination and disappearance of some of the axis cylinders occur, but the thicker axis cylinders persist. Fatty granular cells are numerous in the foci but also hematogenous cells, lymphocytes and some plasma cells are found. The proliferation of the microglia is pronounced.

Of the five cases reported by Montzka [11] two were with necropsy. The clinical onset suggested poliomyelitis. The two fatal cases presented the picture of ascending spinal paralysis with bulbar symptoms; one of these showed signs of complete transverse myelitis of the lumbar region. The two cases with necropsy showed intense perivascular infiltration with polymorphonuclear and lymphocytic cells.

Herrmann [12] also reported a case of acute multiple sclerosis with ascending paralysis, similar to Landry's paralysis. The microscopic examination showed a resemblance to infectious inflammatory processes.

Perdrau [13] remarked that disseminated encephalomyelitis has been recognized for more than fifty years, and its possible relationship to multiple sclerosis was suspected as long ago as 1872 (Westphal). The number of histologic investigations of the central nervous system in the former condition is not large. These descriptions are often marred by the fact that either only a portion of the central nervous system, usually the spinal cord, was investigated or, more often, the histologic methods employed were totally inadequate for the study of nerve tissues. The demyelination in disseminated myelitis is always strictly vascular and symmetrical in distribution. Although similar isolated perivascular lesions are found in acute cases of multiple sclerosis, the large progressive and usually asymmetrical patches of demyelination serve to

11. Montzka, K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **116**:161, 1928.

12. Herrmann: Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:804, 1928.

13. Perdrau, J. R.: Lancet **214**:1201 (June 9) 1928; J. Path. & Bact. **31**:17, 1928.

distinguish it from disseminated myelitis. There is much reciprocal confusion in the literature in regard to these two conditions, and the labels attached to particular cases have varied widely. The occasional involvement of the optic nerves in either condition has served to increase this confusion. Some cases recorded would appear to be transitional forms between these two types. In recent years, cases of disseminated encephalomyelitis seem to have attained almost epidemic proportions. Of the acute infections with which it has been most commonly associated, vaccinia and measles head the list. The first (1912) histologic recognition of this condition when associated with vaccinia was due to Turnbull. A good recent description of a case associated with measles is that of Wohlwill. It is without hesitation, Perdrau stated, that from the accounts to be found in the literature, disseminated (encephalomyelitis) myelitis is a pathologic entity, whatever its association with an acute infection may be. The type which is associated with vaccinia is histologically indistinguishable from the others.

In regard to what Perdrau said, the lesions in my fatal case were strikingly symmetrical on the two sides of the cord. It is difficult to say, on account of the comparatively large size of the lesion, that it was originally perivascular, the lesion had advanced too far for this, and it is impossible to state whether or not perivascular areas of demyelination coalesced to form the large area now present. Perdrau said that in multiple sclerosis isolated perivascular lesions may be found, but the large progressive and usually asymmetrical patches of demyelination serve to distinguish it from disseminated myelitis. It is well recognized that the lesions of multiple sclerosis may be remarkably symmetrical in the two sides of the cord. I have studied a case which shows this in a striking degree. The symmetry occurring occasionally is pictured in a paper by Falkiewicz.[14]

The six cases of acute meningo-encephalomyelitis reported by Brain and Hunter,[15] with a pathologic report of one of the cases by Turnbull, resemble Redlich's cases, especially in the fact that with one exception recovery occurred in all. Fatty granular cells were numerous in the brain but were scarce in the spinal cord. As fat granule cells occur normally during the development of the medullary sheaths, it was impossible, according to Turnbull, to accept the fat granule cells in this case—the child was 3 years of age—as evidence of a pathologic condition or, at any rate, of a specific pathologic condition. English neurologists do not appear to have followed the German in adopting the term gitter cell. The specific changes in the central nervous system in

14. Falkiewicz: Arb. a. d. neurol. Inst. a. d. Wien. Univ. **28**:172, 1926.
15. Brain, W. R., and Hunter, D.: Lancet **216**:221 (Feb. 2) 1929.

the single case examined pathologically were edema, congestion, degeneration of certain groups of ganglion cells and ring hemorrhages.

Brain and Hunter stated the belief that the fulminating onset, cervical rigidity, Kernig's sign and trismus occurring in their cases, with the rapid recovery, distinguish the condition from epidemic encephalitis.

Paresis of individual ocular muscles and pupillary anomalies were not marked in Brain and Hunter's cases, and are in epidemic encephalitis. Sequelae have not been reported in encephalomyelitis disseminata, but the period since the report of cases has not been long enough in some cases to permit any conclusion.

They made three types of cases: 1. Cases characterized by acute degeneration of the ganglion cells of the brain with hyperemia and often marked edema, but without macroscopic hemorrhages. This group includes the cases described by Gordon, Brown and Symmers, and Grinker and Stone. 2. Cases in which the conspicuous feature is multiple macroscopic hemorrhages, so-called "acute hemorrhage encephalitis." This group includes cases of encephalitis following scarlet fever, measles, influenza and pyogenic infection, and cases occurring without any obvious predisposing cause. 3. Cases characterized by perivascular demyelination. This histologic feature has been observed in postvaccinal encephalitis, encephalitis complicating measles, variola, paralysis arising during antirabic treatment and acute disseminated encephalomyelitis.

They thought that there may be no essential pathologic difference between groups 1 and 2, the cerebral manifestations in both being the response to a toxemia, which varies in its effect on nerve cells and blood vessels, so producing varying degrees of edema and hemorrhage.

The areas of degeneration in the encephalomyelitis following vaccination (according to Turnbull [16]) have been remarkably uniform and extend from the cortex of the brain to the lumbosacral cord. The cellular infiltration of lymphocytes and plasma cells in the leptomeninges is described as slight. The most characteristic observations are perivascular and marginal zones of demyelination. Infiltration of the adventitia of vessels in the demyelinated zones is an inconspicuous feature and is frequently absent. The perivascular zones of demyelination may coalesce to form large areas.

Postvaccinal encephalitis is distinct from poliomyelitis and epidemic encephalitis, and belongs to the group of conditions which are characterized by demyelination: certain examples of the disseminated myelitis of Westphal (1874), disseminated encephalomyelitis of later writers, multiple sclerosis and Schilder's disease (encephalitis periaxialis diffusa).

16. Turnbull, H. M.: Brit. M. J. **2**:331 (Aug. 25) 1928.

There can be no doubt that a condition resembling postvaccinal encephalitis has occurred independently of recent vaccination and observed exanthems. Similar histologic changes have been found in diseases of the central nervous system complicating exanthems, especially measles. There can be little doubt that a similar encephalitis may complicate smallpox in view of changes described in the cord by Westphal (1874) in two cases and by Eichhorst (1913) in one. Similar changes have been found in cases in which there was no evidence of recent vaccination or of an exanthem.

The description given by Wohlwill [17] of his cases accords with the observations of Turnbull. He believed that cerebrospinal complications in infectious diseases have increased since the cessation of the epidemic appearance of epidemic encephalitis. Such complications have always been present, but there can be no doubt that they have increased, especially in vaccination, varicella and measles. He gave references to numerous papers on the subject. The clinical manifestations are especially characteristic, but cerebral symptoms predominate; spinal symptoms are less frequent. In his first case occurring in measles he found peripheral proliferation of glia throughout the entire spinal cord, but not in the brain. It varied in width in the cord. He found subependymal proliferation of glia in the lateral ventricle. The perivascular proliferation of glia was present in almost every focus, but it was slight and only a fraction of the thickness of the vessel wall. He spoke of balls from medullary sheaths (Markballen), which stain with hematoxylin, in the degenerated areas. Perivascular lymphocytic infiltration was not present nor infiltration of plasma cells. Death occurred in this child, aged 4, four days after the appearance of involvement of the nervous system.

His second case was also in a child, aged 4; death followed four days after the appearance of nervous symptoms, but six days after the onset of measles. One observation, not present in the first case, was perivascular infiltration with lymphocytes and plasma cells, but this was only in a small number of foci.

His cases, he stated, differ from epidemic encephalitis because the white matter was chiefly affected, and in epidemic encephalitis it is the gray matter which is chiefly affected. In multiple sclerosis the sclerosis is more about vessels, but only about a sharply limited portion, and one may see a vessel entering such a sclerotic patch. His cases more closely resemble vaccine encephalitis. In disseminated encephalomyelitis, he said, the foci are related to vessels, but not as in his cases and more as in multiple sclerosis. In vaccine encephalitis the inflammatory element is more pronounced, but not intense, i. e., lymphocytic infiltration.

17. Wohlwill, J.: Ztschr. f. d. ges. Neurol. u. Psychiat. **112**:20, 1928.

Martin [18] spoke of the frequency with which cases of acute disseminated encephalomyelitis are being encountered in certain parts of London. A number of cases more or less similar have been met with during the last few years in association with vaccination or measles, but until recently they have been rare. In June, 1928, Hunter and Brain were able to report that they had seen six cases within a period of two months.

The cases reported by Martin, four in all, are characterized by the fact first that the symptoms are referable to widely separated, or discrete, parts of the central nervous system, and secondly that they come on in a series of attacks, different parts of the cerebrospinal axis becoming involved suddenly at different times. In none of Martin's cases was necropsy performed.

It is to be expected, he said, that in less severe cases of the disease the malady would not go beyond the stage of one more or less localized lesion, and most of the German cases have been of this type. Many of them presented the picture of a transverse myelitis with sudden onset and rapid recovery. Others at certain stages closely resembled poliomyelitis. The prognosis seems to be favorable for recovery, but recovery may be incomplete and permanent defect remain; no "after-effects," however in the sense of disabilities developing after apparent recovery, have been described.

Greenfield [19] held that the encephalitis of measles is not inflammatory but degenerative. The alterations in the nerve tissues may be chiefly degenerative. He regarded as the most characteristic change the zone of demyelination of greater or less width around many of the small veins. He stated that it is impossible to say that the encephalomyelitis of measles is identical with postvaccinal encephalomyelitis. All one can say is that in some cases no clinical or pathologic differentiation is possible. Whether they also have a relationship to the other demyelinating diseases (multiple sclerosis, diffuse myelitis or Devic's disease and Schilder's encephalitis) is a question which at present is easier to put than to answer. He reported a case. The perivascular softening is with cell exudate. In the early cases the cells may resemble lymphocytes or polymorphonuclear cells. In later cases there is more evidence of fat phagocytosis, and many of the cells are definitely fat granule cells; others are swollen neuroglia cells.

Guillain, Alajouanine, Bertrand and Garcin [20] believed that some cases reported as neuro-myélite optique aiguë are cases of acute or

18. Martin: Lancet **2**:628 (Sept. 22) 1928.

19. Greenfield, J. G.: Proc. Roy. Soc. Med. (Sect. Neurol.) **22**:15 (Jan.) 1929.

20. Guillain, G.; Alajouanine, T.; Bertrand, I., and Garcin, R.: Ann. de méd. **24**:76 (June) 1928.

subacute multiple sclerosis, but they regarded the two conditions as distinct disorders. This designation seems to be employed chiefly by French writers. The lesions they found are: Intense demyelination, varying from one segment to another. The lesions are generally central in the cord near the ependyma. In other places the lesions are peripheral, submeningeal. No tract escapes. The white and the gray matter are irregularly affected. The lesions are not symmetrical and are completely destructive; no axis cylinders are found; myelin, axis cylinders and even the neuroglia framework are destroyed. Gitter cells filled with lipoid particles are accumulated in great numbers; some of these are about the vessels. A striking feature is the disappearance, instead of the hypertrophy, of the neuroglia network. Secondary degeneration occurs. Three necrotic foci were found in the entire cerebrospinal axis; one was in the optic chiasm.

As gitter cells may be numerous in acute multiple sclerosis, it seems to me that the neuro-myélite optique aiguë shows similar lesions differing chiefly in intensity. These writers acknowledge that the distinctions pathologically between the two diseases are difficult to make. Guttmann,[21] in his critical digest on myelitis, mentioned that the neuropticomyélite subaiguë is regarded by most authors as a special form of encephalomyelitis disseminata, but because of involvement of the optic nerve it seems to have a clinical relation to multiple sclerosis.

The subacute necrotic myelitis of Foix and Alajouanine is characterized clinically by progressive amyotrophic paraplegia, at first spastic and later flaccid, the spastic phenomena progressing upward as the amyotrophy and flaccidity develop from below upward; by disturbance of sensation, by albuminocytologic dissociation of the spinal fluid, characterized by massive hyperalbuminosis with slight lymphocytosis, and by subacute evolution leading to death in one or two years.

Pathologically, in two cases necrotic myelitis was found, implicating chiefly the gray but also the white matter, destructive in the lumbosacral region, but it diminished upward and ceased in the midthoracic region. It was associated with intense endomesovascularitis, not obliterating, implicating the extramedullary and intramedullary vessels and causing considerable hypertrophy of the vessels.

These observations apparently have not been confirmed by other investigators, and it is not easy to grasp the pathologic distinctions between this form and the neuro-myélite optique aiguë.

CONCLUSIONS

From a study of my own cases and from the literature the conclusions I have reached are: The distinctions between encephalomyelitis

21. Guttmann: Fortschr. d. Neurol., Psychiat. u. i. Grenzg. **1**:5 (Jan.) 1929.

disseminata and multiple sclerosis at present cannot be sharply drawn. Certain authors, especially the German, assume a close connection between the two diseases. English authors are more inclined to classify encephalomyelitis disseminata with the forms of degenerative processes causing disseminated perivascular demyelination occurring in postvaccinal encephalomyelitis or the exanthems. Some seem to limit the term to such cases. It is probable that certain cases are caused by an unrecognized virus.

DISCUSSION

DR. G. B. HASSIN, Chicago: I wish to call Dr. Spiller's attention to a paper by Dawson, published in 1916, in the Transactions of the Royal Society of Edinburgh. In this paper Dawson points out that in multiple sclerosis the infiltrations of the perivascular spaces may be mainly of fat-granule cells which he demonstrated by such a fat stain as osmic acid. As a matter of fact, with ordinary stains it is sometimes not easy to determine the true nature of the infiltrating cells, and stains like scarlet red or other fat stains are necessary. After listening to Dr. Spiller's paper one may draw the conclusion that the question as to the relationship of disseminated encephalomyelitis to multiple sclerosis is still in a state of confusion. In fact, it is the only conclusion that can be drawn from this paper. Like many other neuropathologists and neurologists, Dr. Spiller is inclined to the opinion that multiple sclerosis is nothing but an extinct inflammatory process; that a long time ago, before the multiple sclerosis manifested itself in the form of patches, scars and similar conditions there was a period when this disease was nothing but an acute inflammatory condition. Such a view seemed to have found support in the recent studies of so-called postvaccinal encephalitis. In this condition are present patches or areas of "demyelination," as the English authors call them. These patches show destruction of the myelin, always associated with a large number of infiltration cells, such as lymphocytes, plasma cells and similar elements. In a recent patch of multiple sclerosis, that is, in the early stages of this disease, one may find similar areas of demyelination, but without such immense infiltrations with hematogenous cells as one finds in the areas of "demyelination" of postvaccinal encephalitis. Aside from such areas one finds in every case of multiple sclerosis patches in the beginning of their formation, and also in a terminal state, which is that of scar formation. These features peculiar to multiple sclerosis not found in any other condition also reflect on the clinical picture.

The first case of Dr. Spiller was one of disseminated encephalomyelitis. The patient got well, for one may recover from disseminated encephalomyelitis, or die when the case is severe. This happened in the second case of Dr. Spiller. In a third type of cases, the patients neither recover nor die. They become cripples or invalids, because of a great number of patches formed. They do not increase in size or in numbers, as they do in multiple sclerosis; they are stationary. For the foregoing reasons the patient is also in a stationary condition, that of helplessness, all his life until he dies from some intercurrent disease. In multiple sclerosis, in contrast, the condition is not stationary, but progressive; it is interrupted by remissions and exacerbations and, what is most important, it may be aggravated

by an inflammatory condition, a typical encephalomyelitis, and, in consequence, is confused with it. This, for instance, occurred in Wohlwill's cases in which both conditions (multiple sclerosis and encephalomyelitis) were combined.

As a rule, however, the differences, clinical as well as pathologic, are great. One is an infection, acute or subacute, and may recur, as was probably the case with the Symmond's patient; the other, multiple sclerosis, is a metabolic disorder resembling amyotrophic lateral sclerosis, subacute combined degeneration of the cord and similar conditions. The few inflammatory phenomena found in multiple sclerosis, in the perivascular spaces of the large blood vessels, are accidental or secondary phenomena. This has been emphasized by Dawson. While Dr. Spiller's conclusions may not be considered final, his contribution is of great importance, for in Europe its subject is agitating the minds of neurologists, neuropathologists and general pathologists, while in this country it has attracted, so far, little if any attention.

Dr. N. W. Winkelman, Philadelphia: Dr. Spiller, as usual, has taken a difficult subject for his study and, as usual, has handled it in his masterly manner. He has called attention to something which in recent literature has tended toward great confusion. I have reference to only one phase of the work that Dr. Spiller has taken up. That is the finding of an occasional vessel with round cells in its perivascular space.

I believe, as he has emphasized, that the mere statement of a fact of this sort is worthless for pathologic interpretation. I believe also that the interpretation of some of the perivascular exudates is again worthless unless verified by differential stains. Any one who has done any pathologic work has seen around tumors, softenings, etc., vessels collared with what seemed to be lymphocytic cells. I have particularly studied these now for some years, and I have come to the conclusion, as Dr. Penfield has, and I might say quite independently, that they are not lymphocytic cells.

The German interpretation of a secondary or symptomatic inflammation is open to considerable doubt. I do not believe many of the cases so designated have had the benefit of differential stains. I do not agree, either, for example, with Michaels and Globus, in their paper on small, round cell infiltration, in which they feel that they have traced the gitter cell from the lymphocyte. The classic work of Hortega does not bear them out.

The question of the differentiation of multiple sclerosis from one or the other acute-appearing foci in the central nervous system has been well covered. The reference to a paper by Dr. Eckel on an acute case of epidemic encephalitis studied very early, within twenty-four hours from the beginning of the illness, is valuable in showing that in many of these cases of purely inflammatory origin, polymorphonuclear cells may be the first type of cell (as it is in poliomyelitis) to appear in an exudate. Later, their place is taken by the lymphocytic cell. Dr. Spiller called attention to the fact that in the future the papers on inflammatory and degenerative conditions of the central nervous system should be and must be studied by differential stains, and their interpretations must be carefully evaluated.

Dr. Spiller: My attention was first attracted to the possibility of multiple sclerosis being an inflammatory condition while I was working in Obersteiner's

laboratory in 1893 and 1894. I found in the anterior horn of the spinal cord in a case of multiple sclerosis that I was studying what appeared to be a lymphocytic infiltration. This observation was regarded as important and was mentioned in a paper published from the laboratory at that time by one of the workers in the laboratory.

Whether this cellular infiltration would be considered as inflammatory in more recent studies I think is questionable. There is no doubt that in my case of acute multiple sclerosis read by title before this association in 1917 and published in 1919, the infiltration in the cerebrum was largely of the microglia type, which would indicate a degenerative rather than an inflammatory process.

EXTENSOR REFLEXES FROM THE KNEE IN RELATION TO THE KNEE JERK AND TO REBOUND*

GRAYSON P. McCOUCH, M.D.
AND
BERNARD J. ALPERS, M.D.
PHILADELPHIA

The present study arose from the observation that the knee jerk could be elicited by striking the inferior edge of the patella from below upward. Since this method of stimulation appears to shorten rather than to stretch the quadriceps, the question arises whether the knee jerk as elicited clinically does not contain other elements in addition to the stretch reflex. Such a possibility is further suggested by the sensation in the region of the subpatellar bursa associated with the patellar reflex.

METHOD

The method employed was copied from the isometric technic developed by Sherrington. Cats were decerebrated by the trephine method, usually after the preparation had been completed under ether anesthesia. The left hind leg was immobilized by section of all muscles inserting in the region of the great trochanter down to and including the quadratus femoris, section of the sciatic nerve, the nerve to the hamstrings, the anterior crural and obturator nerves and the pectineus and iliopsoas muscles. The right leg was similarly prepared except for the anterior crural nerve, the nerve to the hamstrings, and, in the later experiments, the sciatic nerve, which were spared. In the later experiments the popliteal nerve, the anterior tibial and musculocutaneous branches of the peroneal nerve and the tendon of the tibialis anticus muscle were cut. The sartorius muscle was cut near its origin, the tensor fasciae femoris cut free from the fascia and the biceps femoris cut at its insertion. The semitendinosus and quadriceps were freed for recording, and the semimembranosus was cut near its insertion. In some of the early experiments, the obturator nerve was spared and the adductor muscles were cut. The femur was immobilized by two drills, one passing from the great trochanter through the neck of the bone into the hip joint, the other close to the knee and firmly fixed at both ends by rods clamped to upright bars. In the earlier experiments, the pelvis was clamped from the sacrum to the pubic symphysis. In the later experiments, a clamp gripping the pubis between the obturator foramens was substituted. The leg below the knee was fixed at the ankle. Shift in the reflexes from the neck and labyrinth was controlled through fixation by a bar tied

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* From the Department of Physiology and the Department of Surgery, University of Pennsylvania School of Medicine.

* The term "rebound" is here employed to designate the extension which frequently follows the flexion reflex from stimulation of a mixed afferent nerve. It should not be confused with the phenomenon met in cerebellar disease to which Gordon Holmes has applied the same name.

in the mouth. A double isometric myograph, working on the shadowgraph principle, was mounted on a rod clamped through a slot in the table. It was also clamped at two other points to a metal frame supporting a string galvanometer. Though usually giving adequate fixation, the arrangement is inferior in this respect to that employed by Sherrington and his colleagues.[1] Occasionally, as in figure 5 *b*, records were marred by vibration. For recording action currents silver-silver chloride needle electrodes, insulated except at the tip, were employed, as described by Fulton,[1] one in the belly of the vastus externus, the other in the patellar ligament. These led to a gilded quartz string 3 microns in diameter in a Cambridge galvanometer adjusted to give an excursion of string shadow on the film of about 10 mm. per millivolt. In some experiments, the thigh was wrapped in dry cotton surrounding a layer of cotton soaked in Ringer's solution. The cotton was circled by a coil of rubber tubing through which moderately hot water was kept running. In other experiments, muscle exposure was minimized by sewing the skin over all but the area about the knee.

The only unusual feature in the aim of the preparation is the effort to spare as much as possible of the afferent innervation of the subpatellar region. This object was never completely attained. The supply from the external, middle and anterior branch of the internal cutaneous nerves was cut in freeing the quadriceps. The supply from the internal saphenous and from the posterior branch of the internal cutaneous was probably injured in many experiments. The recurrent articular branch of the peroneal nerve was spared in all but the first six experiments in which the sciatic nerve was cut. As far as we are aware, these are the only sources of innervation of the infrapatellar region. To this relative failure to preserve afferent innervation we are inclined to ascribe the high proportion of negative results. For faradic stimulation, the iron core was retained in the inductorium because of the belief that prolongation of the shock favors ipsilateral extensor reflexes;[2] 0.92 ampere was employed in the primary circuit, and both make and break shocks were permitted to reach the nerve. The rate of stimulation employed throughout was 62 make and 62 break shocks per second. Analysis of the records indicates that in many instances the make shocks were ineffectual.

RESULTS

The first six experiments were largely confined to mechanical stimulation. Stretch reflexes elicited by a light glancing tap with a blunt instrument on the thread connecting the quadriceps to its lever were compared with responses obtained on tapping the subpatellar bursa. After a series of such observations, the bursa was painted with and injections were made into it with a 2 per cent solution of cocaine hydro-

1. Fulton, J. F.: Muscular Contraction and the Reflex Control of Movement, Baltimore, Williams & Wilkins Company, 1926, p. 630.

2. Sherrington, C. S., and Sowton, S. C. M.: Proc. Roy. Soc., London, **83**:435, 1910-1911.

chloride (in some experiments, 5 per cent), and the observations were repeated. In two experiments, the application of cocaine did not alter the response from tapping the bursa. Figure 1 shows such a response from one of these experiments in which the bursa was tapped during a series of "spontaneous" contractions of the quadriceps. The reader familiar with the analysis of the knee jerk in the decerebrate cat as elicited by stretch by Ballif, Fulton and Liddell,[3] Fulton and Liddell,[4] Fulton and Pi Suñer [5] and Denny-Brown [6] will recognize the somewhat blunt angle, the "hump" at about half relaxation, the silent period in the electric record between the initial action current and the smaller action current preceding the "hump." In short, the responses from tapping the subpatellar bursa in these two experiments were pure stretch reflexes. In a third experiment, in which 5 per cent cocaine was injected freely into both the bursa and the drill holes, the stretch reflex was progressively exaggerated as a result of the effect of cocaine after absorption. In this case there appeared to be a slight, transient depression of the response

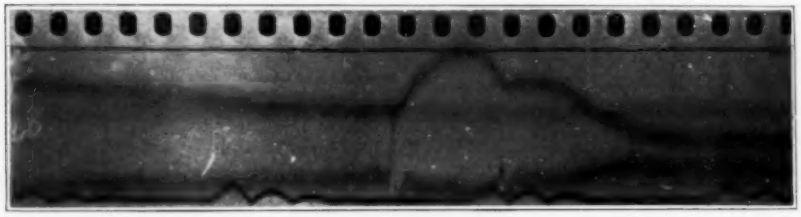

Fig. 1.—Knee jerk from tap to subpatellar bursa in an experiment in which the response was not altered by cocainization of the bursa. Note the slight degree to which the angle is blunted, the brevity of the myotatic appendage, and the quiescence of the galvanometer string both before and after the action current associated with the myotatic appendage. This stretch reflex is superposed on a series of "spontaneous" contractions of the quadriceps. In all the figures, the time below is in 0.2 second.

to tapping the bursa after the exhibition of cocaine, but the peripheral effect, if real, was soon overshadowed by the enhanced stretch reflex. In three experiments, the response to tapping the bursa was abolished after the application of cocaine. In one of these, the quadriceps broke the connection to its lever and was readjusted at a lower initial tension after cocainization. The failure of response to bursal stimulation in this case may be ascribed to the reduction in initial tension as logically as to

3. Ballif, L.; Fulton, J. F., and Liddell, E. G. T.: Proc. Roy. Soc., London **98**:589, 1925.
4. Fulton, J. F., and Liddell, E. G. T.: Proc. Roy. Soc., London **98**:577, 1925.
5. Fulton, J. F., and Pi Suñer, J.: Am. J. Physiol. **83**:554, 1928.
6. Denny-Brown, D.: Proc. Roy. Soc., London **103**:321, 1928.

paralysis of receptors in the bursa. In a second positive experiment, the camera failed to expose the film and no records were obtained. There remains the experiment from which typical records are shown in figure 2. The response to tapping the bursa was almost obliterated after it was painted with 2 per cent cocaine; after cocaine was injected into the bursa, the records showed nothing but the slight mechanical artefact from the tap. The stretch reflex remained unimpaired.

The form of the responses obtained before applying cocaine suggests that they resulted from the summation of bursal and stretch reflexes, the stretch alone being a subliminal stimulus. Electric stimulation afforded a means of isolating the bursal component.

In a second series of eight experiments in which the recurrent articular branch of the peroneal nerve was spared, repetitive induction shocks were employed. In only two of these were records obtained of

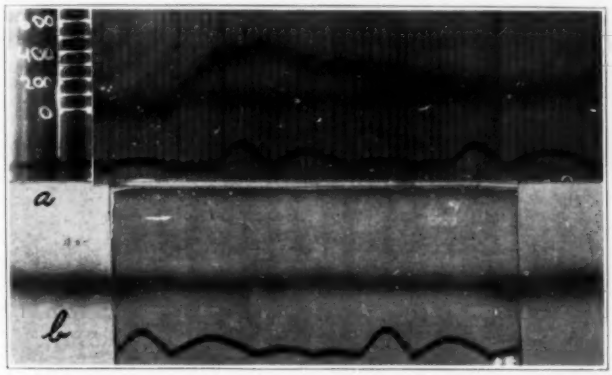

Fig. 2.—Response to tapping subpatellar bursa in an experiment in which cocainization abolished the reflex. *a*, before cocainization. Note the after-discharge; *b*, after bursa has been painted with and injections made into it with 2 per cent cocaine hydrochloride.

responses from such stimulation when the electrodes were applied to the subpatellar bursa. In two other cases (one of them from the earlier series in which the sciatic nerve was cut) positive responses were obtained immediately after the dissection, but could no longer be elicited after the preparation for recording was completed. Such stimulation of the bursa was effectual only when excessively strong currents were employed (coil distances of 5 cm. or less). It is highly probable that the shocks stimulated afferent nerve fibers directly as well as receptors. The possibility that the responses were due to a spread of the current to muscles or efferent nerves may be eliminated for the following reasons: Contraction was confined to the quadriceps, which in our preparations was separated from the point of stimulation by a far greater electric

resistance than many other muscles which did not respond. The only instance we observed of direct contraction from spread of current applied to the bursa occurred in the sartorius with the secondary coil at zero in an animal in which no reflex response was obtained. The latent period of the bursal reflex varied from 0.18 to 0.35 second, intervals implying extensive temporal summation. It was followed by recruitment for from 1 to 2.78 seconds. The end of stimulation was succeeded by an after-discharge which usually maintained the plateau tension for from 1 to 2 seconds and was nearly always well above initial tension at the end of the record which ran in one instance 4.8 and in another 5.6 seconds after the cessation of the stimulus. The electromyogram showed no trace of the rhythm of the induction shocks but consisted of a series of secondary waves continuing without abrupt transition through the after-discharge. The tension developed was low, rarely exceeding 500 Gm. Such a record is shown in figure 3.

Stimulation of the afferent nerves supplying the infrapatellar region by shocks of moderate intensity (coil distance of 12 to 18 cm.) gave responses of a broadly similar character.

The recurrent articular branch of the peroneal gives several small twigs to the upper end of the tibialis anticus muscle, in addition to the branch to the anterior aspect of the tibia and the knee joint. The muscular branches, when cut distally to avoid neuromyal responses, uniformly yield flexion reflexes. In five experiments, we succeeded in isolating the articular division of the nerve and obtained responses such as those shown in figure 4. These records differ slightly from those obtained from stimulation of the bursa. There is an initial relaxation of the quadriceps which we attribute to spread of stimulating current to the afferent fibers from the tibialis anticus already referred to. Stronger currents were required to yield reflex contraction of the semitendinosus. The latency of the extensor reflex is about the same as when elicited from the bursa (about 0.21 second). The tension developed may be considerably greater, presumably owing to the greater number of afferents stimulated. Thus in figure 4 *d*, the shadow of the quadriceps lever passes off the top of the film at a tension of about 1,200 Gm. and crosses it again at a gradual gradient 2.1 seconds after the end of stimulation in a part of the film not shown in the figure. The electromyogram is indistinguishable from that in the reflex elicited from the bursa.

Reflexes were elicited from the main trunk of the peroneal nerve in only a few of the later experiments. In two of these, rebound occurred. In both cases the stimulating electrodes were placed a few millimeters below the recurrent articular branch. Rebound occurred only with shocks strong enough to spread effectively for such a distance. We are impressed by the fact that one instance was in the animal which yielded

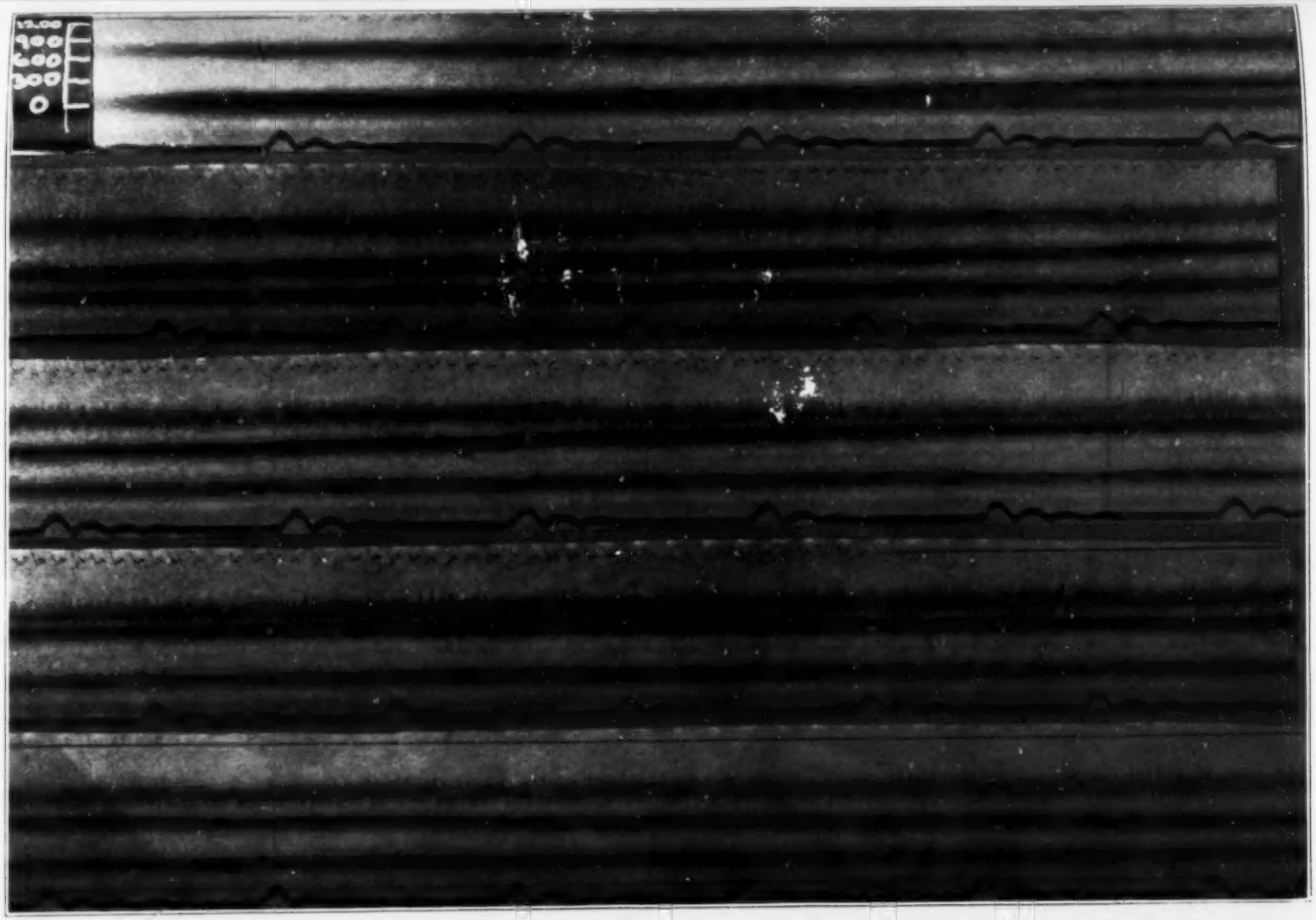

Fig. 3.—Response of quadriceps to strong repetitive induction shocks to subpatellar bursa. Distance of secondary coil from primary coil, 3 cm. Latency, 0.2 second; recruitment, 2.78 seconds; after-discharge was continuing at the end of the record, 5.6 seconds after cessation of the stimulus. Note the absence of rhythm of stimulation in both mechanical and electrical records. The standardization in this figure may be applied to all succeeding figures, with slight error from difference in the base line. In this and all the succeeding figures, the top line indicates stimulus.

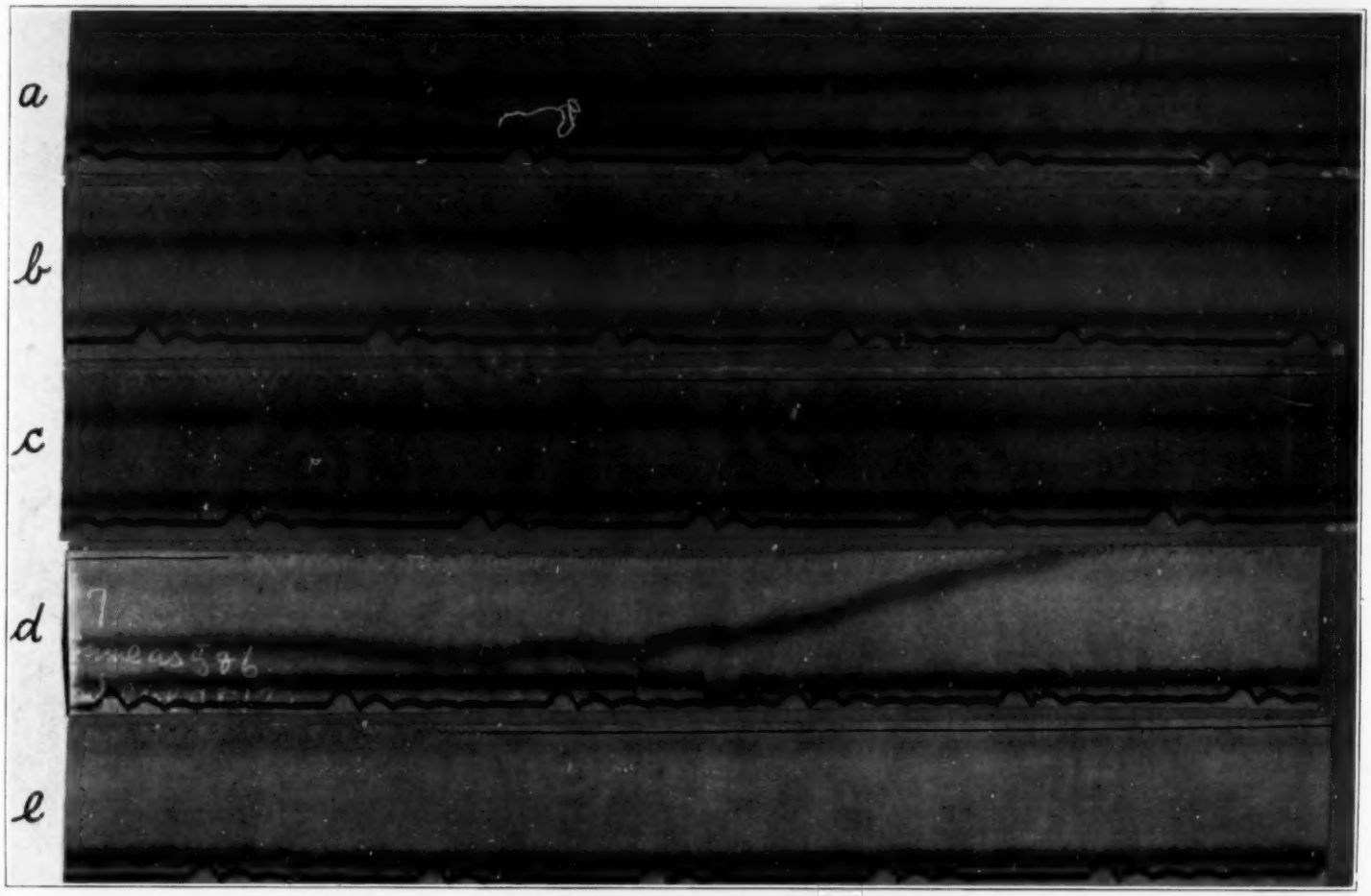

Fig. 4.—Two responses of the quadriceps to stimulation of the recurrent articular branch of the peroneal nerve. *abc* indicates a response with a coil distance of 12.5 cm.; *de*, a response with a coil distance of 12 cm. Note the similarity of this figure to figure 3 except for initial inhibition (due to spread of current to afferents from tibialis anticus?).

the greatest reflexes from the bursa, the other in a case showing strong responses from stimulation of the recurrent articular branch. The similarity of both tension curves and electromyograms in the rebounds to those in the records from stimulation of the bursa and of the recurrent articular branch, even to the degree of tension developed, is evident from a comparison of figures 3, 4 and 5. The record shown in figure 5 *b* was obtained immediately after that in figure 4 *de* with the same strength of stimulus. The smaller rebounds in figure 5 *a* may be compared with figure 3 from the same experiment.

The internal saphenous nerve frequently induced ipsilateral extension when stimulated at or above the level of the knee joint. Such responses

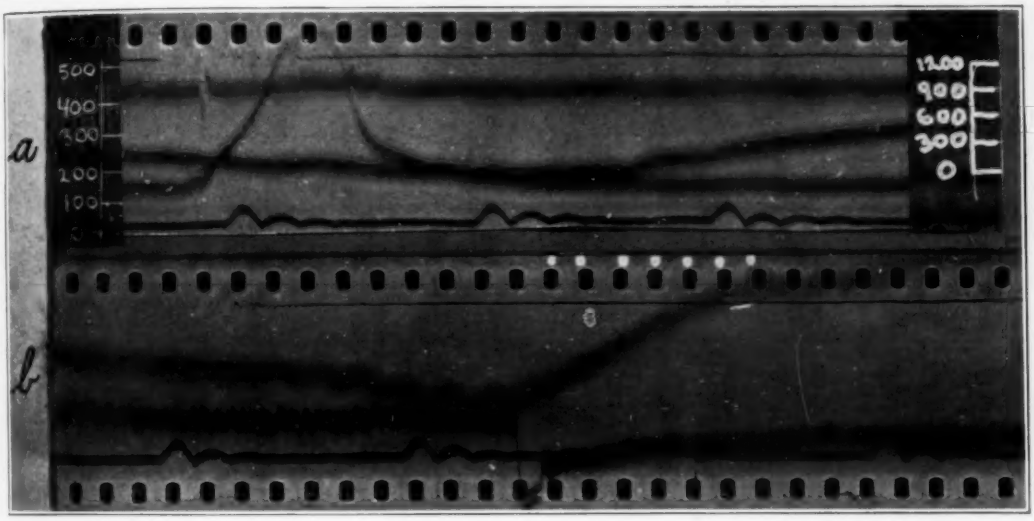

Fig. 5.—Rebounds from stimulation of the peroneal nerve. *a*, from same preparation as that shown in figure 3. Standardization for semitendinosus at left. Standardization for quadriceps at right. Coil distance, 16 cm. *b*, from same preparation as that shown in figure 4. This record was taken just after that shown in 4 *de* and was obtained with the same strength of stimulus (coil distance, 12 cm.). This record is reproduced in spite of the unfortunate artefact from mechanical vibration. Note the correspondence of the rebound to the extensor response in 4 *de*.

were obtained in three of our experiments. In several respects these reactions differ from those from stimulation of the bursa or the recurrent articular branch of the peroneal. The latency is far shorter (usually between 0.02 and 0.04 second). The electromyogram contains primary waves which during a brief period of rising tension follow every fourth or fifth shock, but as the plateau is reached follow the rhythm of stimulation. Primary waves cease with the stimulus, giving way to a series

initial inhibition (due to spread of current to afferents from tibialis anticus?).

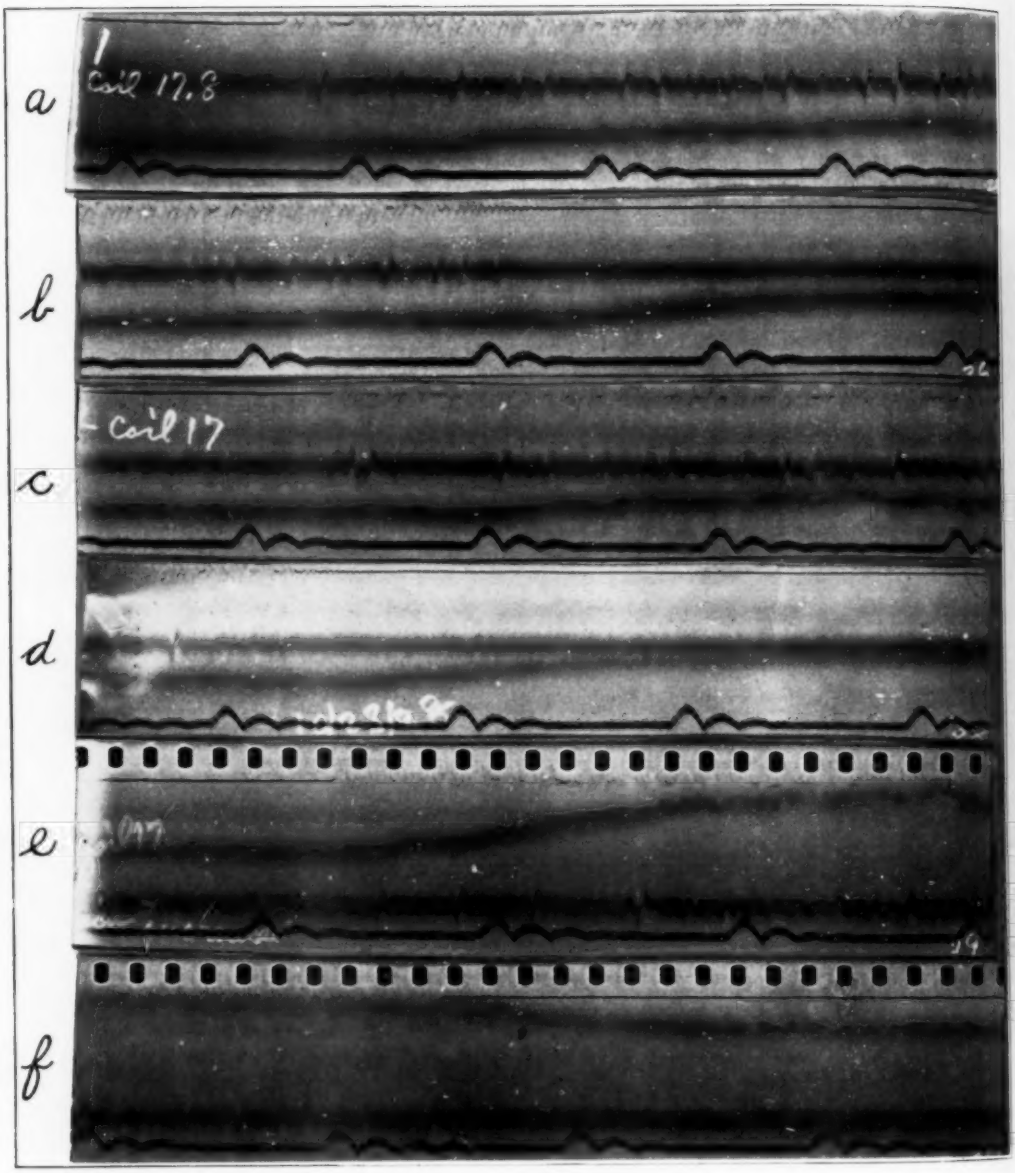

Fig. 6.—Three successive reflex responses of the quadriceps to stimulation of the internal saphenous nerve. *ab*, coil distance, 17.8 cm. (part of the record has been omitted between *a* and *b*); *cd* and *ef*, coil distance, 17 cm. (part of the record has been omitted between *c* and *d*). Between *cd* and *ef*, the initial tension was increased.

of secondary waves during after-discharge. The tension record usually rises in steps in the rhythm of the primary waves of the electromyogram, reaching plateau level within 0.2 second. It frequently exceeds a kilogram. The influence of initial tension is illustrated in figure 6, in which three successive records are shown. The strength of stimulus was the same in the second and third, but before the third the initial tension was increased. In the first two records (*ab* and *cd*) the tension was low

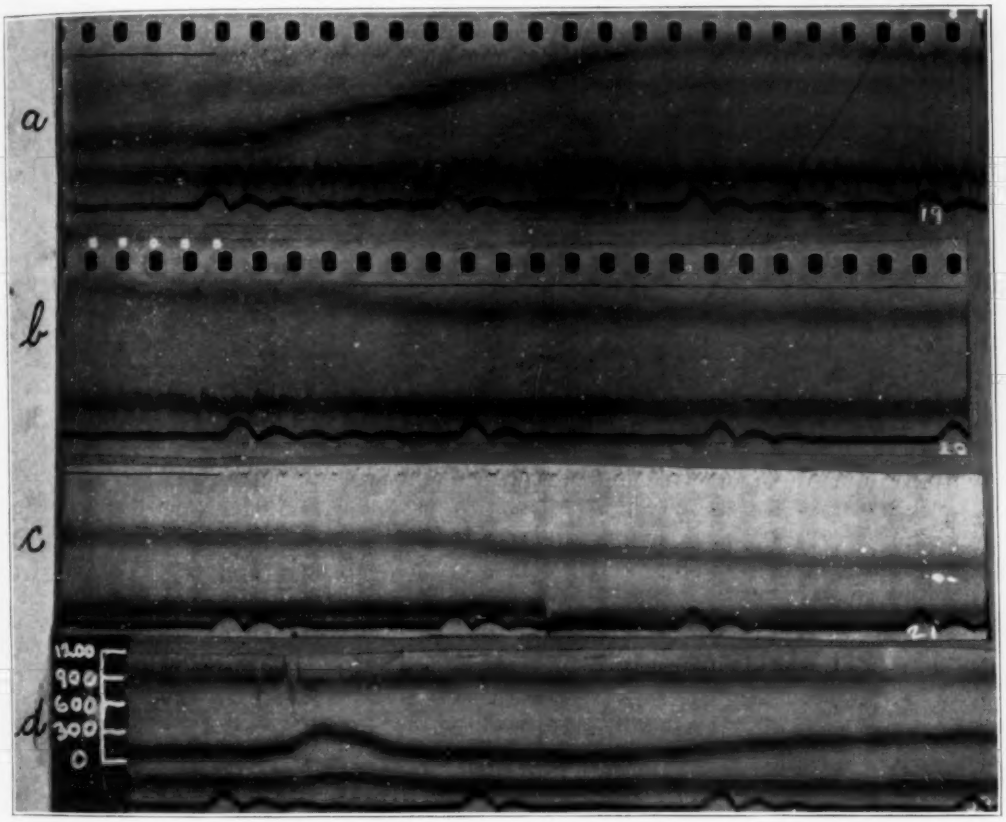

Fig. 7.—Responses of the quadriceps to stimulation of the internal saphenous nerve. *ab*, stimulus above branch to knee (coil distance, 16 cm.); *c*, stimulus below branch to knee (coil distance, 10.5 cm.). *ab* and *c* are from the same preparation as those shown in figures 4, 5 *b* and 6. *d*, stimulus above branch to knee (coil distance, 8 cm.), from the same preparation as those shown in figures 3 and 5 *a*.

throughout the period of stimulation, but rose during the after-discharge in a manner analogous to the rebounds obtained from the peroneal. In the succeeding records (fig. 6 *cf* and fig. 7 *ab*), the tension is far higher during stimulation but falls during the first tenth of a second of after-

discharge to an intermediate level which is maintained to the end of the record. This intermediate tension is considerably greater than that attained during the rebounds in the records at lower initial tension. The duration of the period of falling tension between cessation of stimulation and this second plateau of intermediate tension is approximately equal to the interval in the preceding records between cessation of stimulus and onset of rebound. The increase in the tension attained during stimulation as a result of increase in initial tension exceeds that which would occur in a nerve muscle preparation [1] and is presumably due in large measure to summation with a stretch reflex. The fall in tension on cessation of stimulation may be due to autogenous inhibition (lengthening reaction) which is checked by the onset of rebound.

In the same preparation, stimulation of the internal saphenous below the knee gave a pure flexion reflex. The inhibition of the quadriceps is shown in figure *7 c*.

In another preparation, extensor responses were obtained from both the main trunk of the internal saphenous and its branches at the level of the knee. They resembled those shown in figures *6 cf* and *7 ab* except for the after-discharge, during which tension declined progressively. The third experiment in which ipsilateral extension was elicited from the internal saphenous was one giving responses from the subpatellar bursa (fig. 3) and rebound from the peroneal (fig. 5 *a*). Figure *7 d* shows a response to a brief stimulus to the internal saphenous above the knee. Duration of stimulus is indicated by the primary waves in the electromyogram. The record differs from those in figure 6 in showing a fall of tension on cessation of stimulation followed by rebound after a latency of about 0.2 second.

In spite of variations in response from one preparation to another, the ipsilateral extensions elicited from the internal saphenous resemble those described by other observers.[7] The latency is relatively brief; tension rises rather rapidly to plateau level; primary waves are prominent in the electric record which soon attains the rhythm of the stimulus, and the tension record usually shows steps in the rhythm of these primary waves, at least in the period of rising tension. On the other hand, the extensions from stimulation of the subpatellar bursa and those from the recurrent articular branch of the peroneal differ from ipsilateral reflexes previously described and resemble the crossed extension reflex in a long latency, gradual recruitment, long after-discharge maintained for a considerable time at or near plateau tension, and an electromyogram in which primary waves are either absent or confined to the early phase of recruitment.

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7. Liddell, E. G. T., and Sherrington, C. S.: Proc. Roy. Soc., London **96**:212, 1924. Fulton, J. F., and Liddell, E. G. T.: Proc. Roy. Soc., London **98**:214, 1925.

COMMENT

The analysis of extensor reflexes by Fulton and Liddell [8] throws light on salient features of our results which otherwise would have remained obscure. The extent of our debt will be clear only to those familiar with their work. We can indicate here only one of their conclusions and the type of evidence which led to it. When posterior roots are intact, a crossed extension from stimulation at low frequency shows a tension curve which rises by gradual recruitment, often showing the rhythm of the stimulus and an after-discharge which fails to maintain plateau tension; it yields an electromyogram in which primary waves in the rhythm of the stimulus are prominent during recruitment and often detectable throughout stimulation. After deafferentation, the rise of tension is more rapid and the after-discharge is maintained at plateau level. Primary waves are no longer prominent in the electric record but are smothered by intervening secondary waves. The changes are attributed to release of spinal centers from "autogenetic inhibition" (reflex inhibition from proprioceptors within the contracting muscle or its tendon) of the after-discharge following each primary volley consequent to each afferent volley. "Weak inhibitory stimuli applied to an ipsilateral nerve dissect out the ribs of reflex contraction, i. e., make prominent the rhythm of stimulation through the inhibition of repetitive discharge." [1] This interpretation explains the prominence of primary waves in the rhythm of stimulation in both mechanical and electric records of ipsilateral extension from nerves containing afferents of opposed reflex effect. Thus, even the patellar branches of the internal saphenous contain fibers distributed to skin which probably mediate reflex flexion. On the other hand, the articular portion of the recurrent articular branch of the peroneal, in preparations in which this twig is separate from those to the tibialis anticus, may consist solely of extension-producing afferents, since neither mechanical nor electric records of its reflex indicate the rhythm of stimulation. This view is supported by the fact that we have never observed rebound from the recurrent articular branch alone, though we have observed it from the main trunk of the peroneal and from the internal saphenous.

The interpretation of rebound still presents difficulties, although the investigations of Sherrington,[9] Sherrington and Sowton, Graham Brown,[10] Fulton and Liddell [8] and others have elucidated the conditions

8. Fulton and Liddell (footnote 7, second reference).

9. Sherrington, C. S.: Proc. Roy Soc., London, **76**:160, 1905; **77**:478, 1906; **79**:337, 1907; **80**:53, 1908; Quart. J. Exper. Physiol. **6**:251, 1913.

10. Brown, T. Graham: Quart. J. Exper. Physiol. **4**:331, 1911.

of its occurrence and its reflex pattern. These have been admirably reviewed by Fulton,[1] from whose text the following summary is taken:

> It is easily inhibited and the characteristics of its inhibition closely resemble those of the inhibition of plateau after discharge.
>
> The electrical responses . . . have been found indistinguishable from the string record of plateau after discharge.
>
> It occurs in deafferented muscle.
>
> It occurs most readily in response to strong stimulation of a bare afferent nerve. It has seldom been observed in response to a "natural," that is to say, a homogeneous group of purely inhibitory impulses. Thus, Liddell and Sherrington,[11] when inhibiting the stretch reflex by applying tension to the opposed flexor muscle, did not observe rebound following the inhibition.

Two factors have been invoked in explanation. One is the increase in excitability of a center following its inhibition. The other is the possibility that in stimulation of a nerve containing afferents of opposed reflex effect, the after-discharge of extension outlasts that of flexion. This second factor is suggested by the restriction of observed instances of rebound to stimulation of such mixed nerves and tracts,[12] and by its resemblances to after-discharge. The most serious objection which has been raised to this view is the brevity of after-discharge in the ipsilateral extension reflexes recorded by previous observers. But, as Fulton remarked, "this might conceivably be due to inhibition of that after discharge, the inhibition being unable to quell completely the supported excitation."[1] The responses from stimulation of the subpatellar bursa and of the articular portion of the recurrent articular branch of the peroneal nerve appear to meet the objection and to sustain Fulton's suggestion. Their after-discharge has the duration, degree of tension and type of electromyogram requisite to account for the rebounds from stimulation of the peroneal nerve in the same preparations. We do not wish to imply that postinhibitory exhaltation is not also an important factor; but only that the rebounds in our experiments were of too small magnitude to afford evidence of such a shift in excitability of the center. The fact that rebound usually rises from a background of complete inhibition suggests that the point of origin of the after-discharge, in these reflexes from the region of the knee, is upstream in the reflex arc from the seat of inhibition. Otherwise, a permanent eclipse of after-discharge might be expected. The long latency and gradual recruitment of the reflex accord with such a view.

Our results suggest certain clinical applications. The fact that there is present in the knee jerk an exteroceptive as well as a proprioceptive

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11. Liddell, E. G. T., and Sherrington, C. S.: Proc. Roy. Soc., London **97:** 267, 1925.

12. Bremer, F.: Arch. Internat. Physiol. **19:**189, 1922.

element should be demonstrable clinically. Conditions which involve the nerve supply to the knee joint should cause a change in the knee jerk. To this end, cases of sciatica offer a fruitful source of investigation, especially those traumatic cases in which it can be reasonably certain that only the sciatic nerve is involved. In addition, cases of peroneal palsy with involvement of the nerve above the recurrent articular branch offer an opportunity for the proof of the existence of an exteroceptive element in the knee jerk. It is possible that involvement of the femoral cutaneous nerves to the thigh and of the internal saphenous nerve might alter the knee jerk. Thus far, we have been unable to find cases showing involvement of these nerves. In a random search of the records at the University Hospital, we have found reports of five cases of sciatica with definite decrease in the knee jerk in addition to absence of the ankle jerk in which there is no question of involvement of other nerves. These observations were made by different observers in the course of routine examinations. They suggest that a decreased knee jerk on the side of the sciatica may be of fairly frequent occurrence. Further analysis of the clinical applications of the results presented here must be postponed for a future publication.

SUMMARY

Evidence is presented of the existence of an ipsilateral extension reflex which may be elicited from the subpatellar bursa by either mechanical or electrical stimulation. It is suggested that this reflex may contribute to the knee jerk as tested clinically and that impairment of this component may alter the response to a degree which may lead to errors in diagnosis.

The reflex has been analyzed by synchronous mechanical and electric records taken under isometric conditions from the quadriceps femoris in decerebrate cats. The response to repetitive induction shocks of moderate frequency applied to the subpatellar bursa or to the articular twig of the recurrent articulate branch of the peroneal nerve is characterized by long latency, gradual recruitment to a rather low plateau tension, long after-discharge and absence of rhythm of stimulation in both tension curve and electromyogram. Evidence is presented which suggests that the reflex is concerned in the production of rebound. Extensor reflexes elicited from the internal saphenous nerve above the branches to the knee approximate more closely to those described by other observers from stimulation of the sciatic nerve. The presence of the rhythm of stimulation in these records is ascribed to the presence of afferents of the flexion reflex, which are believed to inhibit repetitive discharge of the center.

Mrs. Evelyn Howard Miller assisted us in several experiments.

THE CEREBRAL CIRCULATION

XI a. THE ACTION OF ACETYLCHOLINE *

HAROLD G. WOLFF, M.D.

BOSTON

Choline and its homolog, acetylcholine, found in tissue extracts,[1] are believed to stimulate primitive receptors or end-organs [2] which are often, but not necessarily, related to the vagus or parasympathetic nerves. The action of choline on the heart, iris and gastro-intestinal system closely resembles that which follows stimulation of the parasympathetic nerves. Whereas its action on blood vessels, vasodilatation,[3] although it follows vagus or depressor nerve stimulation, cannot be said to result directly from the action of parasympathetic impulses on the blood vessel and organs.

The parallelism [4] between the action of acetylcholine and vagus stimulation makes it of interest to determine whether the vessels of the brain, which also dilate on vagus stimulation, act similarly after injections of acetylcholine.

F. Muller,[5] using the Gottlieb modification of the Roy and Sherrington brain oncometer, studied the changes in brain volume and in blood pressure when choline was injected intravenously. He observed that the brain increased in volume in spite of falling blood pressure, and concluded that the brain vessels dilated.

The method used here has been described.[6] In brief, it consists of a small window screwed into a trephine hole in the skull. In the rim of this window are two small holes into which needles are soldered. The surface of the brain is exposed. The window is put in place, and then spinal fluid or Ringer's solution may be irrigated through the needles to wash out the space under the window and to bring the intracranial pressure back to normal. A microscope is placed over the window, and lateral illumination allows an observation of pial vessels up to magnification of 200 diameters. Concomitantly with the microscopic

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* From the Department of Neuropathology, Harvard Medical School.

1. Best, C. H.; Dale, H. H.; Dudley, H. W., and Thorpe, W. V.: J. Physiol. **62**:397, 1927.

2. Hunt, R.: Am. J. Physiol. **45**:197 and 231, 1918.

3. Lampe, W.: Arch. f. exper. Path. u. Pharmakol. **123**:50, 1927.

4. Loewi, O., and Navratil, E.: Arch. f. d. ges. Physiol. **214**:678, 1926.

5. Muller, F.: Pflüger's Arch. f. d. ges. Physiol. **134**:289, 1910.

6. Forbes, H. S.: The Cerebral Circulation: Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

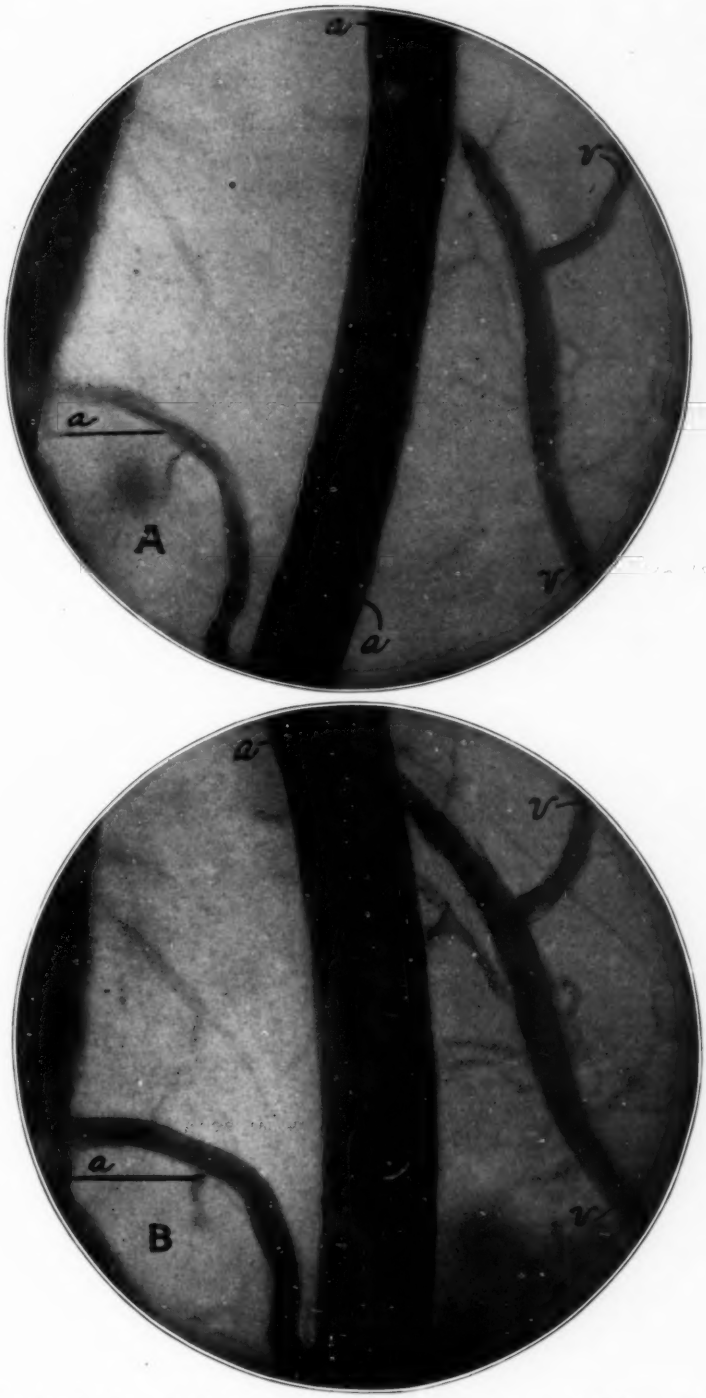

Fig. 1.—Pial vessels demonstrating vasodilatation after acetylcholine: *A*, before intravenous injection of acetylcholine; *B*, after intravenous injection of acetylcholine. Note the dilatation of all blood vessels after the intravenous injection of 0.02 mg. of acetylcholine. In both photographs *a* indicates artery, and *v*, vein. The white spot on the artery is an artefact. Magnification; × 68.

examination, records are made of the intracranial pressure and of the arterial blood pressure in the leg. In this way direct measurements and photographs of the pial vessels were made, and their changes were checked with the changes observed in the general blood pressure and with the intracranial cerebrospinal fluid pressure.

In four cats (average weight, 3.81 Kg.) acetylcholine, in doses of from 0.2 mg. to 0.02 mg., was injected intravenously six times as indicated in the accompanying table. There was an increase in

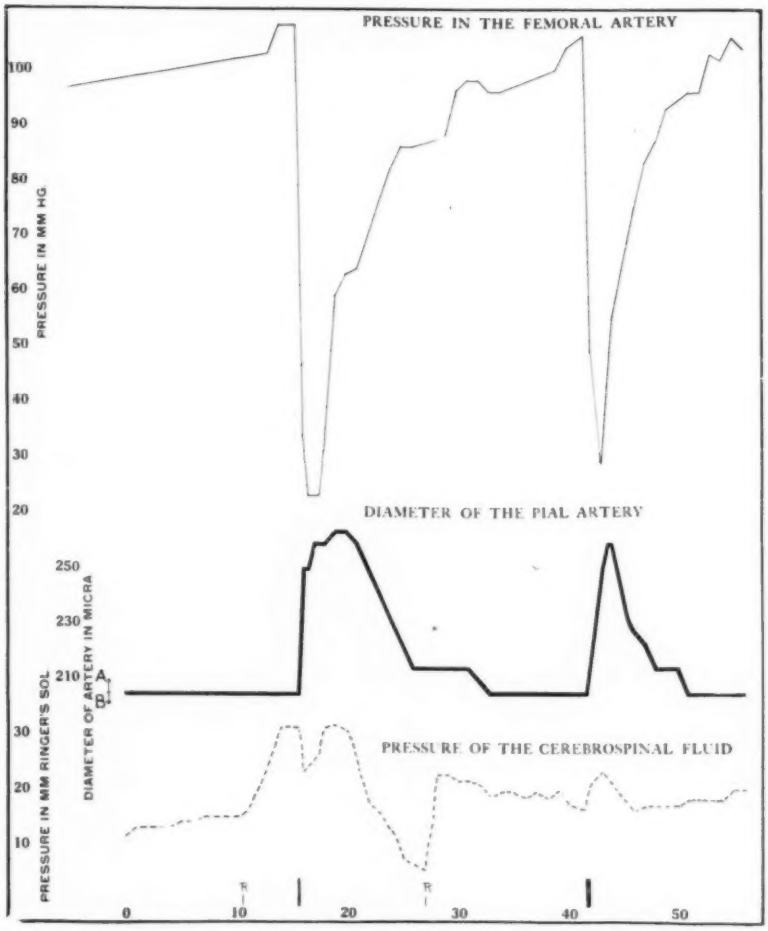

Fig. 2.—Showing the action of acetylcholine on the cerebral circulation. Blocks at the bottom of the chart indicate the time of injection of acetylcholine. Two tenths of a milligram was injected the first time; 0.1 mg., the second. Note the simultaneous fall in blood pressure and increase in diameter of the pial artery, with the slight changes in cerebrospinal fluid pressure. *AB* indicates the probable error of observation. At *R*, Ringer's solution was run into the cistern tube.

Effect of Intravenous Injection of Acetylcholine

Experiment	Dose, Mg.	Diameter of Artery in Microns		Per Cent	Blood Pressure in Mm. of Mercury		Per Cent	Cerebrospinal Fluid Pressure in Mm. Ringer's Solution		Per Cent
		Before	After		Before	After		Before	After	
1*	0.2	207	265.5	32.6	56–7	12	127.3	22–3	14	36.4
1*	0.1	207	261	26.1	53–4	15	71.7	7–8	14	50.0
2	0.02	270	319.5	18.3	44–5	10	126.1	33–5	55–60	67.7
3	0.02	117	130.5	11.5	45–6	38–40	13.3	31–2	37	19.4
3*	0.02	117	135	15.5	49–50	38–40	20.4	35	39	11.4
4†	0.02	207	265.5	32.6	56–7	25	55.4	58	62	6.9
Average	....	...	.....	22.76	.....	.....	69.53	.....	.....	19.8

* See figure 1

† See photographs.

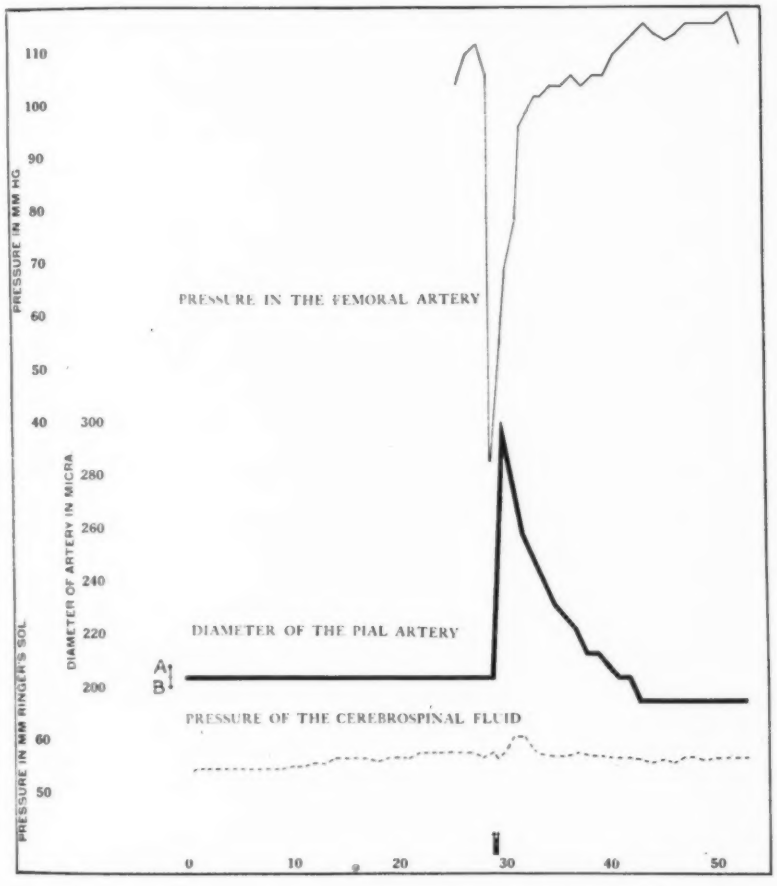

Fig. 3.—Showing the action of acetylcholine on the cerebral circulation. Blocks at the bottom of the chart indicate time of injection of 0.02 mg. of acetylcholine. Note the extreme increase in diameter of the pial artery in spite of the simultaneous fall in arterial blood pressure. *AB* indicates the probable error of observation.

diameter of the cerebral arteries and veins in every instance (fig. 1). With the cerebral vasodilatation there was usually an elevation of cerebrospinal fluid and a fall in the systemic arterial pressure. The cerebrospinal fluid pressure returned to its initial level about the same time that the pial arteries again resumed their former size (fig. 2). In one instance (table, experiment 1) the blood pressure fall was very great, and the cerebrospinal fluid pressure also fell.

The powerful cerebral vasodilator action (fig. 3) probably explains the usual rise in cerebrospinal fluid pressure that occurs coincidently with the increase in the diameter of the vessels of the brain.

With this drug, as with histamine, acetone and lactic acid, cerebral vasodilatation takes place in spite of a great fall in hydrostatic or systemic blood pressure. These observations add further evidence that in the regulation of the diameter of the cerebral blood vessels, the chemical content of the blood is of greater importance than its hydrostatic pressure.

CONCLUSIONS

1. Intravenous injection of acetylcholine causes dilatation of cerebral arteries, veins and minute vessels, usually a rise in cerebrospinal fluid pressure and a fall in systemic arterial pressure.

2. In the regulation of the diameter of cerebral blood vessels, the chemical content of the blood is of greater importance than its hydrostatic pressure.

THE CEREBRAL CIRCULATION

XI b. THE ACTION OF THE EXTRACT OF THE POSTERIOR LOBE OF THE PITUITARY GLAND *

HAROLD G. WOLFF, M.D.
BOSTON

Different investigators seem to have obtained different results from the intravenous injection and local application of solution of pituitary, U. S. P. Dixon and Halliburton,[1] in brain perfusion experiments on dogs, found that pituitary at first constricted and then dilated cerebral arteries. Cow,[2] using rings or sections of surviving cerebral arteries of various animals, found that pituitary caused constriction. Raphael and Stanton [3] measured the changes in the volume of the brain and the pulse through a defect in the skull in man. They concluded that pituitary given intravenously caused cerebral dilatation. Florey [4] directly

Action of Intravenous Injection of 1 cc. of 1: 10 Dilution of Pituitary

Experiment	Diameter of Artery in Microns		Per Cent of Change	Blood Pressure in Mm. of Mercury		Per Cent of Change	Cerebrospinal Fluid Pressure in Mm. Ringer's Solution		Per Cent of Change
	Before	After		Before	After		Before	After	
1	198	173.0	13.6	47	74	57.4	29	35	20.6
2	173	157.5	7.9	67	105	56.7	90	139	54.4
3	126	121.5	3.6	16	42	162.5	32	37	15.6
Average	...	.....	8.3	..	...	92 2	..	...	30.1

observed the cerebral surface (both the convexity and the base) of cats, and observed no change in the size of the cerebral arteries on either intravenous injection or local application of pituitary. Sandor,[5] on studying cerebral blood vessels in the frog by direct microscopic observation, found that pituitary caused constriction which was followed by dilatation. Howe and McKinley [6] noted no change in cerebral arteries in cats after the intravenous injection of pituitary extract.

* Submitted for publication, April 6, 1929.

* From the Department of Neuropathology, Harvard Medical School.

1. Dixon, W. S., and Halliburton, W. D.: Quart. J. Exper. Physiol. **3**:315, 1910.

2. Cow, D.: J. Physiol. **42**:125, 1911.

3. Raphael, T., and Stanton, J. M.: Action of Certain Drugs on Brain Circulation in Man, Arch. Neurol. & Psychiat. **2**:389 (Oct.) 1919.

4. Florey, H. W.: Brain **48**:43, 1925.

5. Sandor, G.: Arch. f. d. ges. Physiol. **213**:492, 1926.

6. Howe, H. S., and McKinley, E.: Cerebral Circulation, Arch. Neurol. & Psychiat. **18**:81 (July) 1927.

The method used has been described.[7] Intravenous injections and local applications of extract of the posterior lobe of the pituitary gland (the brand used was pituitrin, obstetric, Parke Davis and Company) have been made. Cats averaging 3.6 Kg. in weight were used.

The action of pituitary on pial vessels was determined on seven animals. In four the drug was applied directly to the pial surface, and in three an intravenous injection was made. One cubic centimeter

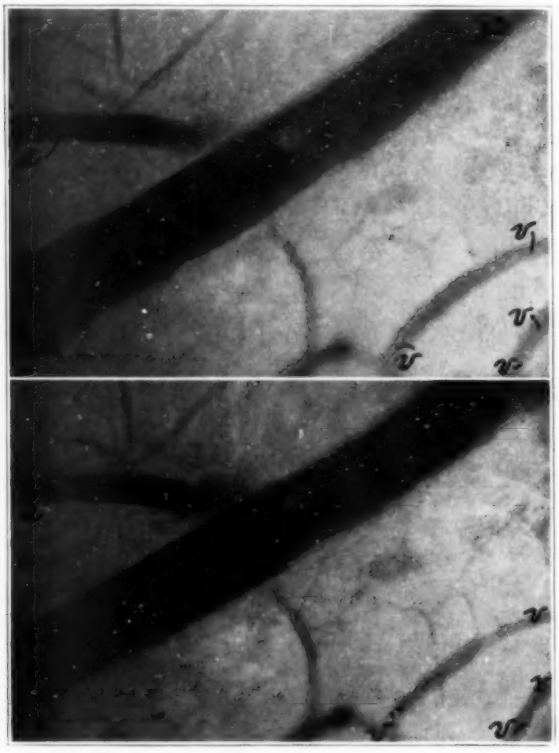

Fig. 1.—Pial vessels: *A*, before injection of pituitary; *B*, after intravenous injection of 1 cc. of a 1:10 dilution of pituitary. The photograph was taken just after the blood vessels were beginning to contract and at the height of the rise in systemic arterial pressure. There is a slight constriction of both arteries and veins. In both photographs, *a* indicates artery and *v*, vein. Magnification; × 68.

of a 1:10 dilution in Ringer's solution was injected intravenously. Two cubic centimeters of a similar dilution was irrigated locally. Vasoconstriction occurred in all three animals into which the drug was intravenously injected, and in two of the four in which it was applied

7. Forbes, H. S.: The Cerebral Circulation: Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:751 (May) 1928.

locally. The greatest constriction after intravenous injection was 15.4 per cent, the least 3.6 per cent and the average 8.3 per cent (see table). After local application no change occurred in one, and dilation in an other.

When local application of pituitary caused cerebral arterial constriction, the venules also constricted. No change in arterial or cerebrospinal fluid pressure was observed under these circumstances. The

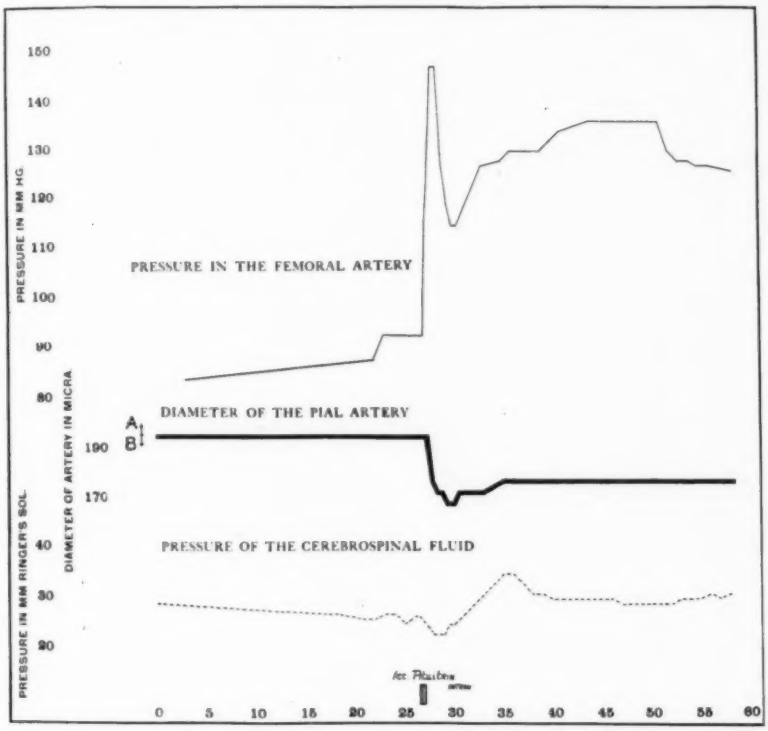

Fig. 2.—Action of extract of the posterior lobe of the pituitary gland on cerebral arteries. The small block at the bottom indicates the time of injection of 1 cc. of a 10 per cent solution of pituitary. With the rise in systemic arterial pressure, the pial artery became narrower. It remained so in spite of the elevated blood pressure. The cerebrospinal fluid pressure, after a slight fall, rose and remained slightly elevated during the period of the rise in the blood pressure. Arrow *AB* indicates the probable error.

vasodilatation after local application of pituitary in one experiment, and the absence of any reaction in another, may result from the action of adulterance (preservative) or a slight acidity of the solution.

Pituitary injected intravenously caused a rise in arterial blood pressure and vasoconstriction of the pial arteries (fig. 2). This was

accompanied by a brief and slight fall in cerebrospinal fluid pressure during the period of maximal cerebral vasoconstriction, and was followed by a rise which was maintained as long as the elevation in systemic blood pressure continued. The initial fall in cerebrospinal fluid pressure was not always present.

When the systemic arterial blood pressure rose to a considerable height after the intravenous injection of pituitary, the cerebral arteries at first dilated. Shortly after the maximum rise in systemic blood pressure or during the beginning of the fall, the cerebral arteries became visibly narrower, and reached their maximal constriction shortly thereafter. The greatest rise in blood pressure was 163 per cent, the least 56 per cent and the average 92 per cent.

Without quantitative methods, the minute changes in diameter that frequently occur after intravenous injection could readily be overlooked. The vasoconstriction is never striking, but the change in diameter, though small, is definite.

CONCLUSIONS

1. Extract of the posterior lobe of the pituitary gland causes constriction of pial arteries, arterioles, veins, venules and minute vessels.

2. Vasoconstriction after intravenous injections of pituitary indicates that the diameter of the brain vessels is influenced more by the chemical content of the blood than by its hydrostatic pressure.

THE CEREBRAL CIRCULATION

XI C. THE ACTION OF AMYL NITRITE *

HAROLD G. WOLFF, M.D.

BOSTON

That the cerebral vessels respond by dilatation to the inhalation of amyl nitrite has already been noted by various investigators. Schuller,[1] directly observing the surface of the brain through the intact dura, noted that amyl nitrite caused (in rabbits) dilatation of all cerebral vessels. Mosso [2] measured the volume of the brain and the pulse through a defect in the skull in three patients. He concluded that since amyl nitrite always caused an increase in the bulk of the brain, the drug must have caused dilatation of cerebral vessels. Hurthle [3] drew conclusions concerning the diameter of the cerebral vessels from measurements of blood pressure in the circle of Willis in rabbits and cats. He inferred from his observations that amyl nitrite caused cerebral dilatation. Biedl and Reiner [4] employed a similar method, measuring also venous output. They, too, concluded that amyl nitrite caused cerebral vasodilatation. Shepard,[5] using in human beings (with cranial defects) an apparatus similar to that of Mosso, obtained the same results. Hirschfelder [6] observed the size of retinal and cerebral vessels, and measured coincidently the systemic blood pressure. He observed vasodilatation in the retina and in the brain when amyl nitrite was inhaled. Raphael and Stanton [7] also, in measurements on man similar to those of Mosso and Shepard, concluded that amyl nitrite caused cerebral vasodilatation. Florey,[8] observing cerebral vessels directly through the open skull of cats, noted vasodilatation with the use of amyl nitrite. Leake and others [9] photographed cerebral blood

* Submitted for publication, April 6, 1929.

* From the Department of Neuropathology, Harvard Medical School.

1. Schuller, M.: Berl. klin. Wchnschr. **11**:294, 1874.

2. Mosso: Ueber den Kreislauf des Blutes im menschlichen Gehirn, Leipzig, 1881.

3. Hurthle, K.: Arch. f. d. ges. Physiol. **44**:561, 1889

4. Biedl, H., and Reiner, M.: Arch. f. d. ges. Physiol. **79**:158, 1900

5. Shepard, J. E.: The Circulation and Sleep, Experimental Investigations, New York, The Macmillan Company, 1914.

6. Hirschfelder, A. D.: J. Pharmacol. & Exper. Therap. **6**:597, 1914-1915.

7. Raphael, T., and Stanton, J. M.: The Action of Certain Drugs on Brain Circulation in Man, Arch. Neurol. & Psychiat. **2**:389 (Oct.) 1919.

8. Florey, H. W.: Brain **48**:43, 1925.

9. Leake, C. D.; Loevenhart, C. S., and Muehlberger, C. W.: Dilatation of Cerebral Blood Vessels as a Factor in Headache, J. A. M. A. **88**:1076 (April 2) 1927.

vessels through the open skull before and after the action of the drug, and then measured the photographic plates. Injecting glyceryl trinitrate intravenously, a drug similar in action to amyl nitrite, they noted an average vasodilatation of 21 per cent in each of sixteen dogs. Kochmann and Römer [10] noted an increase in intra-ocular pressure with the fall in arterial pressure after inhalation of amyl nitrite. A similar relationship is observed (figs. 1 and 2) between arterial pressure and cerebrospinal fluid pressure in our experiments. Among those who have experimented with the drug on the blood vessels of the brain there is very general agreement.

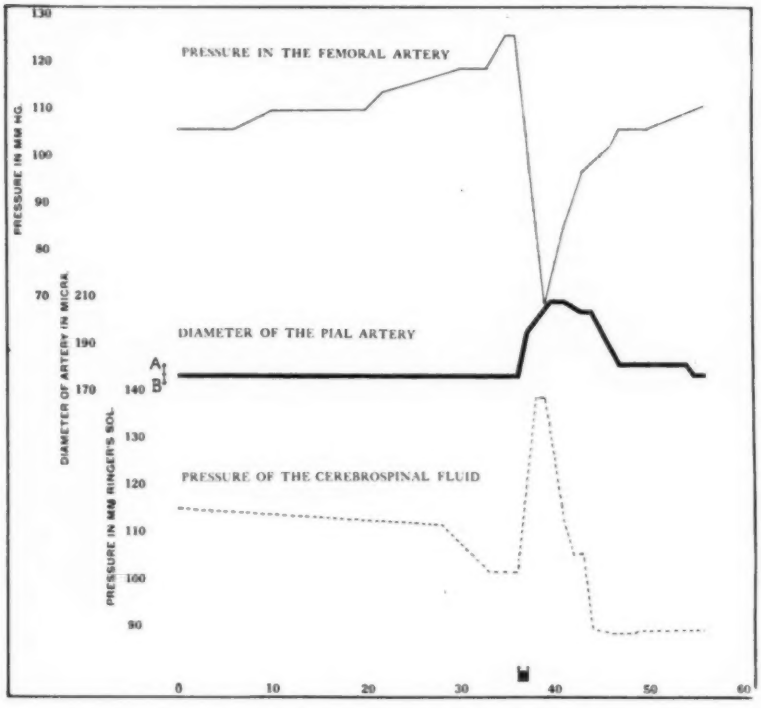

Fig. 1.—The action of amyl nitrite. The block and arrows at the bottom of the chart indicate when the amyl nitrite was inhaled. Note the sharp drop in systemic arterial pressure and the simultaneous increase in diameter of the pial artery and the pressure of the cerebrospinal fluid. Arrow *AB* indicates the probable error of observation.

The following observations are presented because of their quantitative nature. Employing photography and micrometric observations together with measurements of cerebrospinal fluid and of systemic

10. Kochmann, M., and Römer, P.: Arch. f. Ophth. **88**:527, 1914.

arterial pressure, we are now able to make more accurate statements concerning the action of amyl nitrite on cerebral vessels.

The method used has been described.[11] Amyl nitrite was inhaled six times by five cats for from one to four minutes. The pial artery dilated, the blood pressure fell and the cerebrospinal fluid pressure rose in every instance (fig. 1). It is to be noted that the veins and minute vessels as well as the arteries dilated (fig. 3).

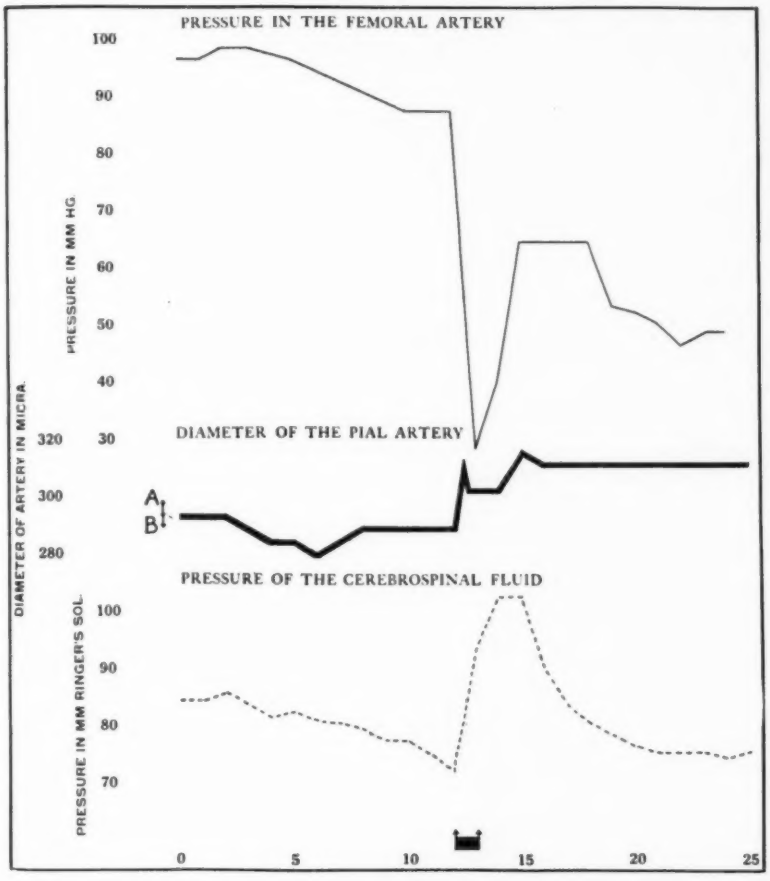

Fig. 2.—The action of amyl nitrite. The block and arrows indicate the period of inhalation of amyl nitrite. With the fall in systemic arterial pressure, the cerebral artery dilated. The cerebrospinal fluid pressure increased during the period of cerebral vasodilatation. Note that the diameter of the pial artery remained dilated after the immediate effects of the drug were over. Arrow *AB* indicates the probable error of observation.

11. Forbes, H. S.: The Cerebral Circulation: Observation and Measurements of Pial Vessels, Arch. Neurol. & Psychiat **19**:751 (May) 1928.

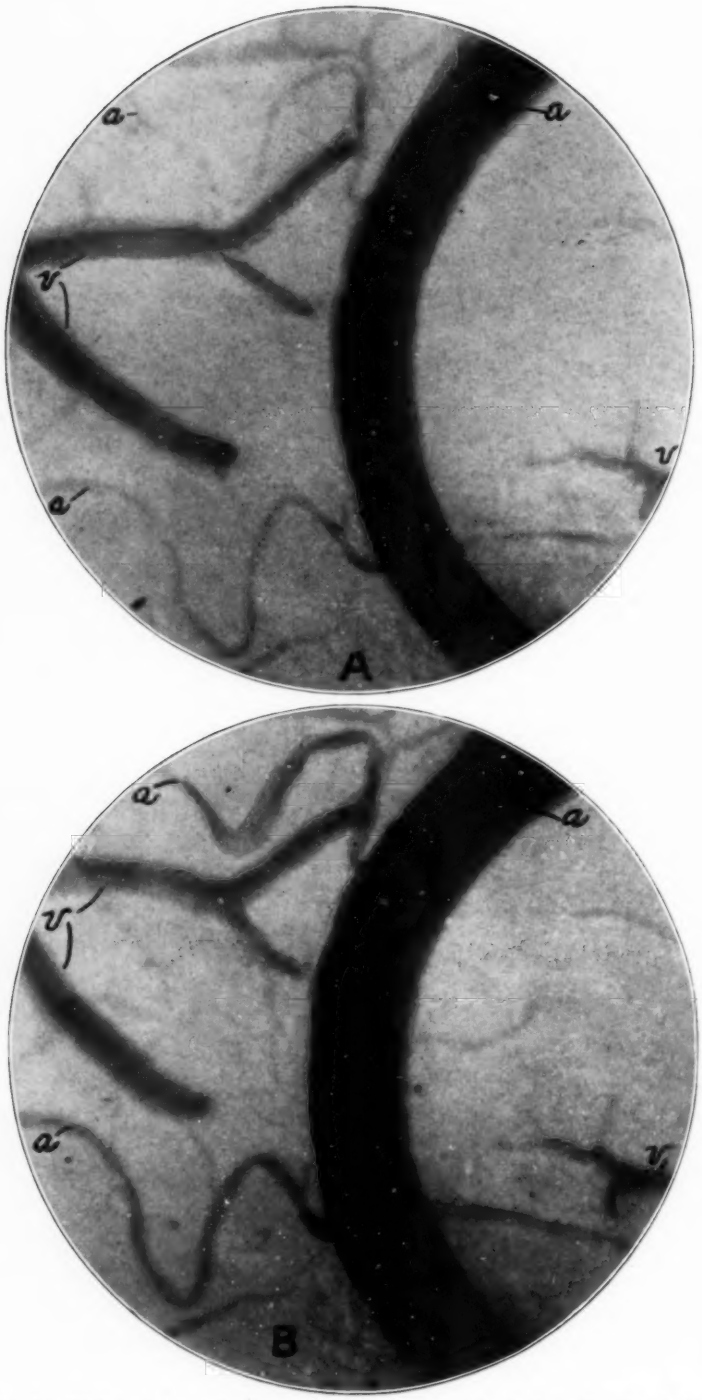

Fig. 3.—Pial vessels: *A*, before inhalation of amyl nitrite; *B*, after inhalation of amyl nitrite. Note dilatation of all the blood vessels. The photograph was taken when the systemic arterial pressure had fallen to its lowered level. In both photographs *a* indicates artery and *v*, vein. Magnification; × 68.

The color of the blood often changed during the inhalation of amyl nitrite; the usual brilliant scarlet of the arteries and purple of the veins became tinged with brown or chocolate color. The animals were dyspneic by this time.

During the systemic vasodilatation, the arterial blood pressure fell promptly and remained low during the whole period of cerebral vasodilatation, during which time the cerebrospinal fluid pressure stayed high. With the gradual rise in blood pressure, the cerebral arteries again became narrower, and the cerebrospinal fluid pressure tended to return slowly to its initial level.

The action of the drug on the walls of the cerebral blood vessels is probably similar to its action on blood vessels elsewhere in the body.

The Effect of Inhalation of Amyl Nitrite

Experiment	Dose, Minims	Diameter of Artery in Microns		Per Cent	Blood Pressure in Mm. of Mercury		Per Cent	Cerebrospinal Fluid Pressure in Ringer's Solution		Per Cent
		Before	After		Before	After		Before	After	
1.....	½	153.0	189	23.5	..	..	....	...	...	....
1.....	4	126.0	162	28.6	74	32	60.0	...	...	....
2.....	1	292.5	319	9.2	35	15	58.3	74	104	44.4
3.....	1	67.5	108	60.0	54	26	50.9	...	...	....
4.....	1	144.0	157	9.4	..	..	....	44	87	91.2
5.....	1	180.0	211	17.5	63	35	46.1	104	139	33.3
Average.	..	.....	...	24.7	..	..	53.8	...	...	59.6

The action of the drug may be complicated (in cats, at any rate) by the formation of methemoglobin. Interference with the normal function of hemoglobin may explain the prolonged vasodilatation sometimes observed in these experiments (fig. 2), by producing a state of partial asphyxia. Asphyxia, as in carbon monoxide poisoning, causes prolonged cerebral vasodilatation.[12]

CONCLUSIONS

1. Inhalation of amyl nitrite in cats causes dilatation of cerebral vessels.

2. Associated with the cerebral vasodilatation, there is a fall in systemic arterial pressure and a rise in cerebrospinal fluid pressure.

12. Forbes, H. S., and Wolff, H. G.: The Cerebral Circulation: The Action of Carbon Monoxide, to be published.

HYPERPYREXIA PRODUCED BY BATHS

ITS EFFECT ON CERTAIN DISEASES OF THE NERVOUS SYSTEM *

H. G. MEHRTENS, M.D.

AND

P. S. POUPPIRT, M.D.

SAN FRANCISCO

Hot baths in the treatment for disease is one of the oldest therapeutic procedures. The ancient Egyptians, Greeks and Romans not only used this mode of treatment, but worked out elaborate devices for its administration. The therapeutic possibilities of many of the thermal springs of Western Europe were discovered by the Romans. In this stage of the clinical application of the bath, attention was centered largely on its temperature and little on the fever produced in the patient. This situation not infrequently resulted in fatalities.

Not until physiologists undertook a systematic study of the results of experimentally induced fevers was it possible to make a rational clinical application. A large mass of facts has been collected,[1] but little clinical use has been made of this information.

Meanwhile, the importance of fever was being emphasized in another direct line of clinical investigations. Intercurrent fevers had been known since the earliest times to exercise a benign effect on certain neurologic conditions. Later, the injection of foreign proteins, vaccines, intraspinous treatments and the inoculation of malaria and rat-bite fever, all pointed to the importance of fever as a therapeutic measure. Schamberg's [2] experiments in sterilizing chancres by immersing the animals in hot baths again called attention to hot baths as a means of producing therapeutic fevers. The time seemed ripe to reevaluate the clinical effect of hyperpyrexia on neurosyphilis and other neurologic conditions, some of the modern apparatus being utilized for recording temperature.

Our material consisted of 70 patients, and 900 baths were given. Work was carried on for about one and a half years. The patients were of both sexes, ranging in age from 17 to 70 and including such unpromising risks as marasmic, arteriosclerotic and nephritic patients with hypertension.

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* Submitted for publication, May 1, 1929.

* From the Neuro-Psychiatric Clinic, Stanford University Medical School.

* Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 27, 1929.

1. Bazett, H. C.: Physiological Responses to Heat, Physiol. Rev. **31**:531, 1927.

2. Schamberg, J. F., and Rule, A. M.: Studies of the Therapeutic Effect of Fever in Experimental Rabbit Syphilis, Arch. Dermat. & Syph. **14**:243 (Sept.) 1928.

METHODS EMPLOYED

The Apparatus.—In the beginning of the work, an ordinary bath tub and bath thermometer were found sufficient equipment to produce a satisfactory fever. Later, after the suggestion of Rosanoff,[3] we utilized the continuous bath. This gave more comfort to the patient and, at the same time, allowed a simple regulation of the temperature of the bath. An ordinary mouth thermometer was used to measure the patient's temperature. In cooperative patients and at lower temperatures for the bath, this method gave accurate results, but at higher temperatures accompanied by rapid mouth ventilation or in stupid noncooperative patients, the mouth temperature was frequently found to be not only inaccurate but misleading (fig. 1). In such a case, had the mouth temperature been considered

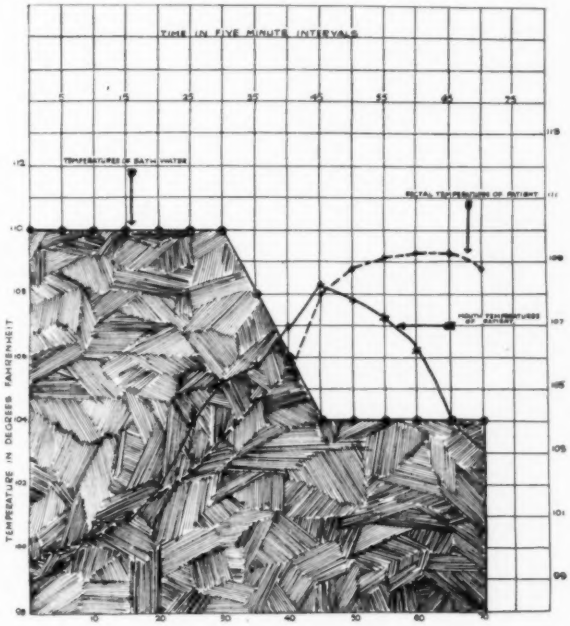


Fig. 1.—An illustration of the inaccuracy of mouth temperatures in noncooperative patients.

correct and the bath temperature been raised accordingly, a calamity might well have resulted. To obviate this possibility, a thermocouple was utilized to obtain rectal readings at intervals of five minutes. A comparison of mouth and rectal temperatures shows (fig. 2) a close correlation between the curves. Whenever there is a discrepancy between the observations, the rectal readings are the most dependable. The local cooling of the nasopharynx made the mouth temperature the least reliable as an index of general bodily temperature.

Height of Fever.—In the treatment for neurosyphilis it seemed desirable to raise the patient's temperature as high as is consistent with comfort and safety. The mouth temperatures were never less than 104 F. and preferably from 105 to

3. Rosanoff, A. G.: Thermo-Therapeutic Technique, Am. J. Psychiat. **7**:489, 1927-1928.

107 F. Patients varied greatly in their ability to tolerate high temperatures. Many needed encouragement during the first treatment; subsequent treatments were always easier to give. Our experience convinced us that the poor results obtained by Hollingsworth [4] in his treatment of a group of neurosyphilitic patients were due not only to the relatively low temperatures employed, but also to the short period of time during which these temperatures were maintained.

Technic.—Our technic consisted of immersing the patient in a bath at 110 F. With timid patients or on the occasion of the first bath, the temperature was sometimes started at 105 F. Ordinarily, 110 F. was maintained until the temperature of the patient reached a point within a degree and a half of the fever desired. Then the temperature of the bath water was gradually reduced until it corresponded with the temperature of the patient. The ordinary bath lasted one hour, but when indicated, it is feasible to maintain the patient's fever for another hour by wrapping him in blankets and placing a few hot water bottles in the bed. Liquids may be administered by mouth, but they must be hot.

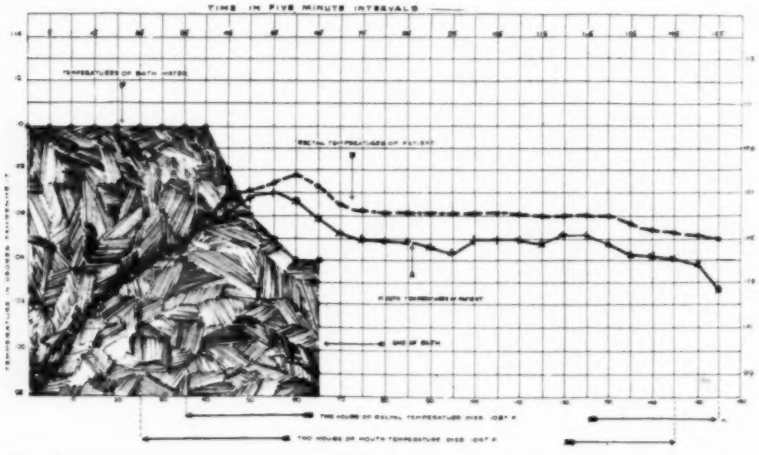


Fig. 2.—Mouth and rectal temperatures of a patient, as well as the temperature of the bath water, during a two-hour treatment by hyperpyrexia.

Frequency of Baths.—In the interest of economy most of our patients received one bath daily. A few patients received two daily, but we were not convinced that this was good practice except in unusual cases. The ordinary series was fourteen baths, followed by a period of rest. At times, twice this number were given consecutively with no added difficulty. In some conditions other than neurosyphilis, it seemed preferable to give a bath every other day, or rarely, every third day.

RESULTS IN GENERAL

Following a bath all patients were somewhat fatigued, but many walked to their rooms. Each patient lost from 3 to 5 pounds (1.3 to 2.2 Kg.) in weight, but under proper dietary supervision the loss was

4. Hollingsworth, M. W.: Hot Baths in Late Syphilis, Arch. Dermat. & Syph. **18**:736 (Nov.) 1928.

made up by the next morning. Most patients end a series of fourteen baths with a gain in weight. The pulse mounted regularly as shown in figure 3. No irregularities or marked variations of rate were noted.

The blood pressure in the majority of cases was reduced. The average reduction per bath was 50 mm. systolic and 20 mm. diastolic. The following day, the pressure rose to its former level. In a series of baths, the reduction was relatively slight. In rare instances, the systolic pressure was increased.

The basal metabolic rate was difficult to take in the bath. When obtained, it showed an increase of from 80 to 100 per cent.

Blood Picture.—The hemoglobin and red cell count, when influenced at all, tended to show increases. The reticulocytes showed a uniform increase of from 2 to 3 per cent.

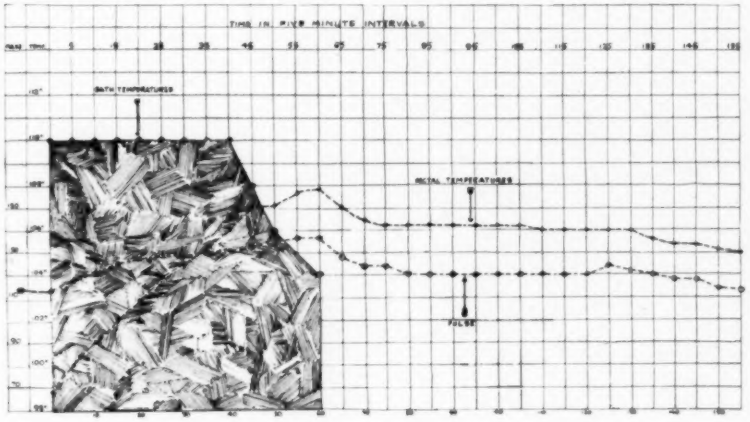


Fig. 3.—Variations in the pulse during hyperpyrexia.

Psychologic Reactions.—The reactions of the patient in a hot bath showed some interesting features. In baths at temperatures between 98 and 102 F., all the patients were calm and cooperative; between 102 and 103 F., they frequently showed signs of restlessness and anxiety, and made efforts to elevate the limbs out of the water; from 103 to 105 F., the patients were quieter and rather apathetic; between 105 and 107 F., mild confusion frequently occurred, extending in unusual cases for an hour after the patient's return to bed.

Serology.—The serologic changes followed roughly what we had learned to expect from our experience with malaria. The Wassermann reaction of the spinal fluid was frequently diminished in intensity, and the colloidal gold reaction often changed from a paretic to a tabetic type. In one patient who had been treated over a period of five years, a persistent paretic type of colloidal gold reaction was changed, by one

series of fourteen baths, to a tabetic type. The serologic change following the fever brought on by the baths came on rapidly, frequently within a month after the completion of a series of baths. The serologic changes produced by malaria came on later, averaging six months.

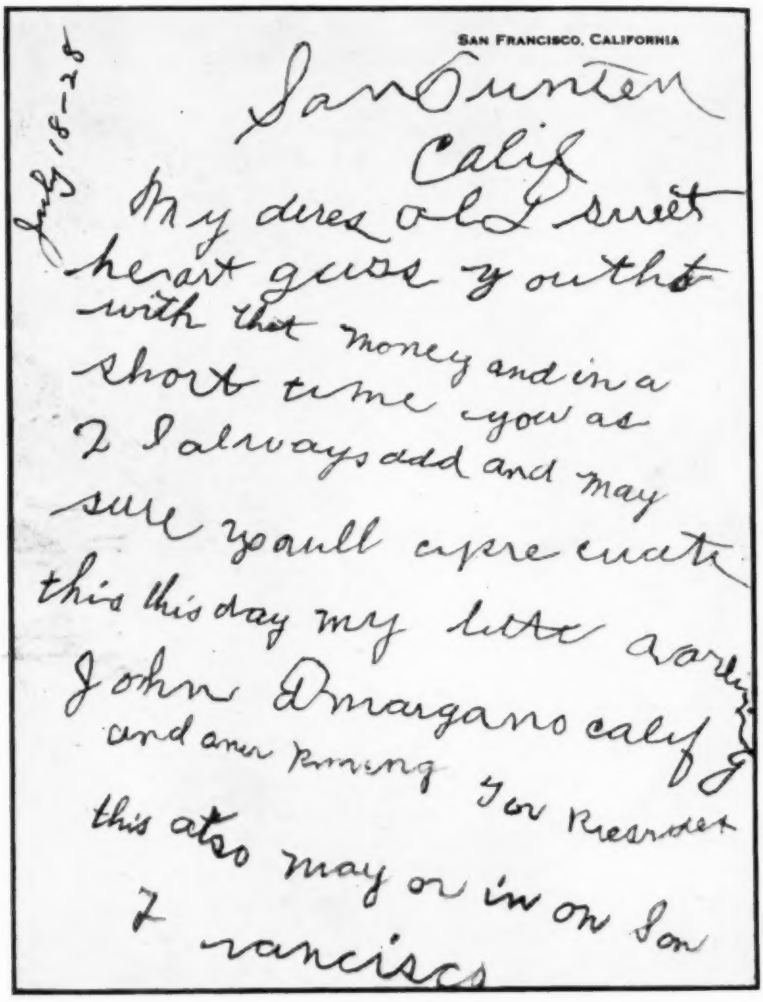
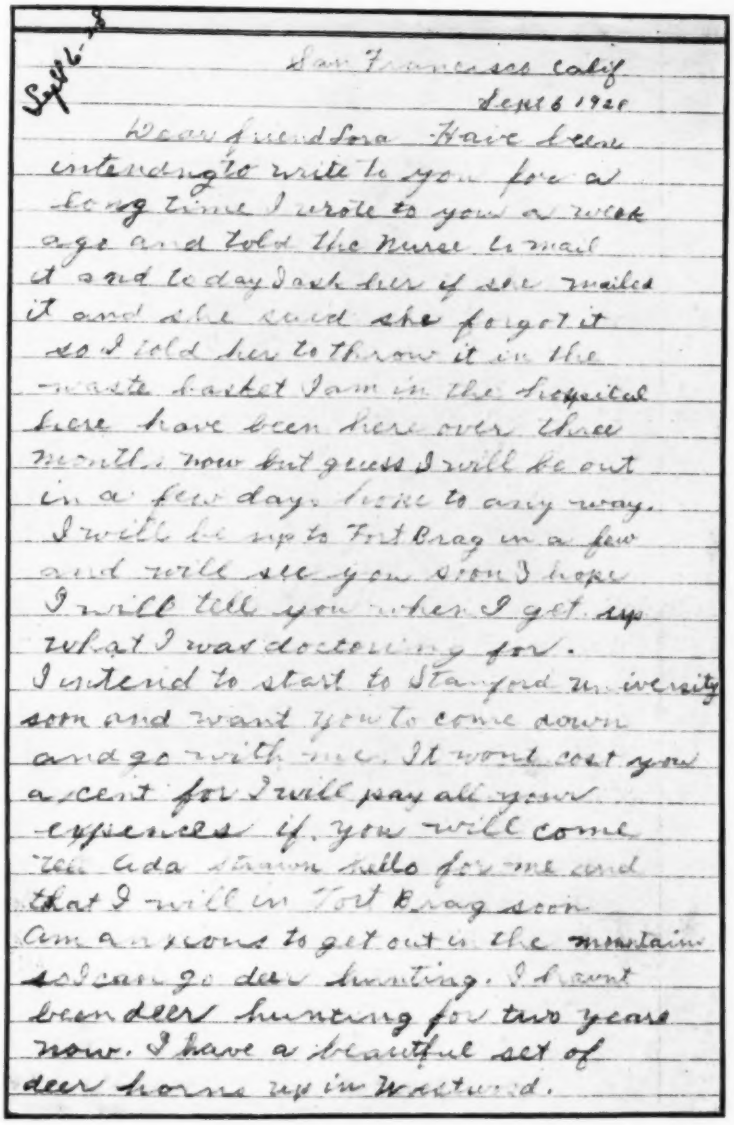


Figure 4 A

Fig. 4.—Improvement in letter writing by a paretic patient treated with hot baths.

As yet we have noted no case in which the spinal fluid has been rendered entirely normal solely as the result of fever from baths.

Permeability of the Meninges.—The permeability of the meninges was increased by fever produced by baths. Using Malamud's modi-



Sept 6-20

San Francisco Calif
Sept 6 1920

Dear friend Sra Have been
intending to write to you for a
long time I wrote to you a week
ago and told the Nurse to mail
it and today I ask her if she mailed
it and she said she forgot it
so I told her to throw it in the
waste basket I am in the hospital
here have been here over three
months now but guess I will be out
in a few days here to any way.
I will be up to Fort Bragg in a few
and will see you then I hope
I will tell you when I get up
what I was doctoring for.
I intend to start to Stanford University
soon and want you to come down
and go with me. It wont cost you
a cent for I will pay all your
expences if you will come
Tell Ada Strawn hello for me and
that I will in Fort Bragg soon
Am a anxious to get out in the mountains
so I can go deer hunting. I have
been deer hunting for two years
now. I have a beautiful set of
deer horns up in Westwood.

Figure 4 B

fication of Walter's technic, we showed that the permeability quotient in all cases was lowered. In order to achieve this increased permeability it was necessary that the hyperpyrexia be greater than 103 F., be continued for at least thirty minutes and be repeated on at least five successive days.[5]

Clinical Results.—Paresis: Eleven patients were treated. Two recovered sufficiently to return to work; four showed marked clinical improvement, but are not able as yet to earn a living; three showed slight clinical gains, and two were unimproved. Psychometric rating did not demonstrate improvement after treatment even in the patients able to return to work. Improvement following treatment can be divided into stages. The effect observed after two or three exposures to high temperature is sometimes startling. The patient may become completely oriented, cooperative and quiet. This effect we were forced to ascribe to some local circulatory change in the brain. The later continued improvement might be attributed to the real healing process (fig. 4).

The condition of the spinal fluid was improved in six cases, particularly in the colloidal gold test. The tendency for a curve of the paretic type to change to one of the tabetic type was noticeable. Patients resistant to other methods of antisyphilitic treatment were especially liable to show altered reactions to the colloidal gold test when exposed to hot baths. The series is too small and the time too short to draw any conclusion about end-results.

Tabes: The condition of every patient in the twenty cases was improved in some way. Many patients were helped symptomatically. This was particularly true of the "burnt-out" cases showing no positive changes in the spinal fluid. Lightning pains, gastric crises and Charcot joints yielded to hot baths more readily than to any other therapy that we had previously used.

Figure 5 shows the relief obtained in an especially severe case of gastric crisis. We had entirely failed to help this patient on several entries by using large doses of morphine. His attacks usually lasted for several days. Hot baths controlled the pain in about twenty minutes. The amelioration of symptoms following hot baths was not always permanent. Lightning pains and gastric crises tended to recur, particularly after intercurrent infections. The relapses were further apart than the original attacks, less severe and more amenable to another series of baths. Ten patients with tabes treated with routine anti-

5. Mehrtens, H. G., and Pouppirt, P. S.: Effect of Hyperpyrexia, Produced by Baths, on Permeability of the Meninges, Proc. Soc. Exper. Biol. & Med. **26**:287, 1929.

syphilitic therapy were given heat therapy in addition. The results in this small series seemed better than those obtained with either the anti-syphilitic therapy alone or the heat therapy alone.

Encephalitis (Parkinson Type): Nine patients were treated. This group did not give the generally favorable results found in the neuro-syphilitic patients. In a majority of the patients treated, tremor was reduced, spasticity lessened and ocular crises modified. Occasionally improvement was sufficient to enable a patient confined to a chair to go back to a sedentary employment. Relapses after treatment was discontinued were common, but about half of the patients retained their gains. On the whole, the general health of the patient was noticeably benefited by hot baths.

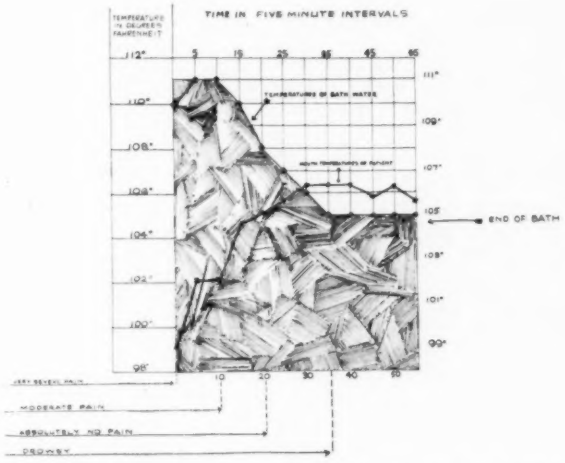


Fig. 5.—Treatment in a case of gastric crisis and its effect on symptoms.

Combined Sclerosis: In the three cases studied we were prepared for transitory results at most. Annoying paresthesias were readily eliminated with a few baths, but tended to return after a few weeks or months. Muscular weakness ordinarily was not favorably influenced. One patient benefited sufficiently to return to hard manual labor.

Miscellaneous Conditions: A group of patients whose chief complaint was pain were treated. Those suffering with arthritis, myositis, neuritis and radiculitis, all seemed to get relief more promptly and completely than by any other physiotherapeutic means at hand. It is for this group of patients that hyperpyrexia may, in the hands of the general practitioner, give the most satisfactory results, as the pathologic state is still amenable to treatment.

Amyotrophic Lateral Sclerosis: Three patients were treated without any perceptible benefits.

Excited Psychotic Patients: It was found that baths giving a mouth temperature of 104 F. upward, prolonged over an hour, tended to act in a sedative fashion, definitely more so than with the controls at 98.6 F. The baths were frequently followed by restful sleep. In many of the patients who could be induced to take proper nourishment, a gain of weight was noticed. At first it seemed that exhaustion might be a possible explanation of the patient's subsequent relaxation; later we were inclined to believe that we must be dealing with other factors, for after a series of fourteen baths no evidence of weakness could be detected.

COMMENT

In comparing the results produced by hot baths and the malarial treatment, the latter is simpler. It requires less cooperation on the part of the patient. The temperature can be maintained for several hours out of the twenty-four. There may be valuable factors in the toxemia apart from the fever. Fever produced by baths is under perfect control. It can be maintained at any degree or for any length of time up to two hours; it may be applied on alternate days or even on every third day if necessary. Baths may be continued daily for at least six weeks and the patient may still gain in weight and maintain his strength. They may be applied along with antisyphilitic therapy; it is even probable that the hyperpyrexia tends to intensify the therapeutic effect of the antisyphilitic medication.

CONCLUSIONS

1. Fever resulting from baths can be maintained for one or even for two hours without danger to the patient.

2. It is necessary to raise the mouth temperature to at least 104 F., sometimes as high as 107 F., and to maintain it for one hour in order to obtain clinical results.

3. Most patients gain in weight, and show an increase in hemoglobin and reticulocytes and in their permeability quotient.

4. Neurosyphilis seems to offer the most favorable field for treatment by hyperpyrexia. The results compare well with those obtained by malaria therapy. Frequent amelioration of individual symptoms was obtained in Parkinson's syndrome following encephalitis, as well as in combined sclerosis. Pain resulting from minor disturbances in muscle, nerve and joints proved especially amenable to treatment by heat. No results were obtained in amyotrophic lateral sclerosis.

5. Fever therapy may be used to intensify the effect of antisyphilitic medication.

INCIPIENT PARKINSONISM

A DIAGNOSTIC TRIAD FOR ITS EARLY RECOGNITION *

A. M. ORNSTEEN, PH.G., M.D.
Associate in Neurology, University of Pennsylvania Medical School; Associate in Neurology, Temple University Medical School
PHILADELPHIA

Ordinarily, the recognition of the parkinsonian state of chronic epidemic encephalitis is unattended by difficulty or uncertainty. Yet, in my experience, incipient and fragmentary forms of the disorder have offered diagnostic difficulties because of the uncertainty and paucity of physical signs. With this experience in mind, I have closely scrutinized and studied many patients suffering with varying degrees of parkinsonism to determine the constancy of early symptoms and signs.

Subjective evidence of ill health antedates the appearance of objective signs in most instances; an exception will be noted in the case reported. At this stage of experience with this comparatively new disease, however, one cannot venture a diagnostic structure of symptoms alone.

Of the physical signs, it has been found that postural and tonetic changes in the hands occur earliest and with greatest constancy and more often unilaterally. In order to facilitate their ready recognition, three tests have been used to great advantage, and are herein presented as a diagnostic triad: (1) finger posture in repose; (2) finger spacing of the outstretched hands, and (3) thumb-forefinger test.

DESCRIPTION OF SIGNS

1. *Finger Posture in Repose.*—The patient is asked to stand at attention but thoroughly relaxed. The observer's attention is then directed to the posture of the hands which are in repose by the sides. In the normal subject, the palm faces the thigh, and the fingers are slightly flexed at all joints, the thumb being slightly flexed at the metacarpophalangeal joint and extended at the other. The important observation is that the posture is symmetrical on the two sides (fig. 1). In early parkinsonism, the hand on the affected side shows an increase of the degree of flexion at the interphalangeal joints (fig. 2). This is a positive finger posture sign, while the normal is spoken of as a negative finger posture sign.

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* Read at a meeting of the Philadelphia Neurological Society, Jan. 25, 1929.
* From the Neurological Departments, University of Pennsylvania and Temple University Medical Schools and Jewish Hospital.

2. *Finger Spacing of the Outstretched Hands.*—With both upper limbs of the patient fully extended in front, palms down, the attention of the observer is directed to the fingers to note the relative position in space of the individual digits to one another as to uniformity of spacing and bilateral symmetry. In the normal person spacing is usually uniform and symmetrical. The fingers are either all closely adducted, except the thumb, which may be in either adduction or abduction, or all widely separated. Then again, the spacing in each hand may be uneven, but this irregularity is symmetrical in the two hands with only slight variations (fig. 3). In the abnormal state, definite asymmetry between the two sides occurs, with greater irregularity noted in the affected hand (fig. 4).

3. *Thumb-Forefinger Test.*—The patient is asked to hold both hands aloft in front of his face, with all fingers in the palms except the thumb and forefinger. He then is asked to perform rapidly interrupted move-

Figure 1

Figure 2

Fig. 1.—Normal posture. Note the symmetry of the two sides.
Fig. 2.—Abnormal posture on the left side.

ments of touching the forefinger to the thumb, with the digits making wide excursions. Normally, the act is performed symmetrically on the two sides (fig. 5). In the abnormal state, one notes a definite limitation of agility, definite reduction in the amplitude of the movement and a tendency to earlier exhaustibility on the affected side, thus constituting a positive result for this test (fig. 6).

OBSERVATIONS ON CERTAIN VARIATIONS

Normal Variations.—In a posture of repose, the flexion in the fingers in some normal persons increases slightly in each succeeding finger from the second to the fifth. The forefinger is often seen to be in a more anterior plane than the other fingers. In the outstretched hands, the fifth finger may be strongly abducted while the remaining fingers are adducted. A frequent spacing seen is slight separation of the second

and third, somewhat greater between the third and fourth and much more between the fourth and fifth. The position of the thumb apparently is of little value. In all cases, regularly or irregularly spaced, the two hands are symmetrical. Regularity is more frequently observed than irregularity.

Variations in the Abnormal Hand.—With the increased flexion of the distal phalanges may be observed, in rarer instances, a straight metacarpophalangeal segment, i.e., absence of the slight normal flexion. There occurs also a full extension and separation of all fingers with strong abduction of the fifth finger. A third variation in the posture of the fingers in repose may be an increase of flexion at the metacarpophalangeal joints with no change in the interphalangeal joints, thus bringing the thumb in close contact with the forefinger. In the normal posture, the thumb and forefinger are separated.

Figure 3

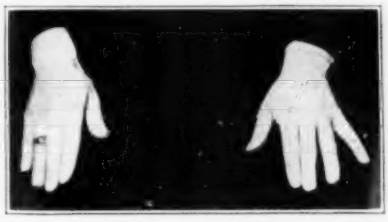


Figure 4

Fig. 3.—Normal spacing; note the symmetry.

Fig. 4.—Abnormal spacing; note the asymmetry on the left.

In the spacing test, one may see many variations. For instance, several cases have been observed in which there was a change in the relative positions of the digits in the vertical plane, the fifth, fourth and third, each being in a plane successively lower. Or the forefinger alone may be in a higher plane than the others. These changes in the vertical plane are associated with irregularities in lateral spacing. Again, there may be close adduction of all fingers in the affected hand, while the normal or less affected hand shows a more or less even and natural spacing. An oft-associated phenomenon is an incomplete pronation of the hand with incomplete extension at the elbow on the affected side.

In making the first two tests, the observer must be careful not to permit the patient to become "hand conscious," because automatic, associated overtones may be released into the muscles. It is self evident that

when deviations from the normal occur symmetrically on the two sides, greater care must be used in their evaluation; when these changes are unilateral, their significance is definite.

The third sign is most constant in its appearance and occurrence, the first being next in order and the second least. The first and third signs are sufficient to impress one with the encephalitic or parkinsonian background. Yet, it will be noted that the signs are not presented in the order of their importance; instead they are described in the order recommended for their elicitation. It is advisable that no active voluntary movements of the hands precede the first test, which depends wholly on relaxation, because of the possibility of the persistence of overtones in the flexor muscles.

COMMENT

To convince oneself of the significance of these signs, one has but to take a definite case of unilateral parkinsonism and compare the two

Figure 5

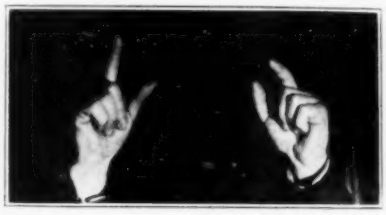


Figure 6

Fig. 5.—Height of normal excursion; equal on the two sides.
Fig. 6.—Limitation of excursion on the left.

hands. Their diagnostic usefulness is materially diminished in the presence of the more readily recognized signs, such as characteristic facies, body attitude, limb postures and loss of associated arm swing in walking. Before these gross changes develop, however, the elicitation of this triad of signs gives the clinician a more tangible basis for a diagnosis of incipient paralysis agitans.

REPORT OF AN ILLUSTRATIVE CASE

To illustrate the value of these signs the following case is cited:

R. S., a girl, aged 14, with no antecedent history of acute infections that might suggest acute encephalitis, and with no symptoms, past or present, of encephalitic nature, began to have a twitch of both eyelids on the left about six weeks before this examination. The lids twitched rhythmically and coarsely about two times a second. The condition was a definite myoclonic tic of the orbicularis palpebrarum, rhythmically narrowing the palpebral fissure without closing the eye.

The character of this hyperkinetic phenomenon suggested its striatal nature. For this reason careful search was made for evidence of beginning parkinsonism, especially since blephorospasmodic manifestations are frequent associated phenomena of parkinsonism.

The facies was normally mobile in the expression of emotion, with perhaps a slight suggestion of fixity. Retraction of the right corner of the mouth in showing the teeth was slightly delayed as compared to the left. Walking appeared normal and the associated arm swing was unimpaired on either side. On the strength of these signs alone, therefore, one would hesitate to diagnose beginning parkinsonism. But with positive changes in the posture of the fingers in the right hand (increased flexion), asymmetrical finger-spacing (irregular in the right hand) and definite changes in thumb-forefinger movements on the right, such a diagnosis could be entertained. In her left hand, all tests were negative. A further confirmatory observation was an increase of both knee reflexes, more so on the right. Ocular convergence power was not limited. Two months after this examination, she developed diurnal somnolence and impairment of ocular convergence.

SUMMARY

1. Fragmentary forms of incipient parkinsonism of chronic encephalitis, in my experience, have been only tentatively so classified because of the uncertainty and paucity of physical signs.

2. A careful study of the early signs and symptoms in many cases of the disorder reveals the fact that subjective manifestations antedate physical signs in most instances, but that the former are too protean to be reliable as diagnostic criteria.

3. Of the physical signs, postural and tonetic changes in the hands have been found to be most constant and earliest in their appearance. Therefore, a triad of physical signs is herein described and offered as an aid to the early recognition of incipient parkinsonism.

HABITUS LIPODYSTROPHICUS WITH AFFECTIVE PSYCHOSIS (HYPOMANIC EXCITEMENT) *

F. I. WERTHAM, M.D.
BALTIMORE

In the investigation of the morphologic constitution, the variations in fat distribution in women are of special importance. It has been found that the different body types, e. g., those described by Mills, Sigaud and Kretschmer, are far less clear in women than in men. Bauer, who has used the type system of Sigaud in a large number of cases, even thought this system unsuitable for the classification of the female habitus. He considered the distribution of subcutaneous fat a much more characteristic sign. Other observers, however, have found these morphologic types useful in the study of women, and the types of Mills and Kretschmer have been indicated in women by anthropometric methods dealing only with skeletal proportions.[1] That it is more difficult to differentiate these morphologic types in women than in men is undoubted.

Another point that adds to the importance of variations in fat distribution in women is the fact that marked anomalies in the distribution of fat, especially in conjunction with other "growth disorders," have the significance of dysplastic signs. Anomalies in fat distribution in men, e. g., that of the eunuchoid type, are usually easily recognizable. In women this is much more difficult because of the wider range and many degrees of fat distribution generally found. For this reason, the biometric evaluation of "growth disorders" (as far as they are concerned with subcutaneous fat) in their correlation with disease is much more difficult in women than in men.

In a previous publication, attention was drawn to a type of habitus, so far found only in women, which seems to deserve separate consideration.[2] The chief characteristic of this type of habitus is a marked incongruity in the fat deposition of the upper and the lower parts of the body, marked thinness above the waistline, combined with marked obesity below the waistline. The contrasting form, obesity in the upper part of the body combined with a definite lack of fat in the lower part of the body, has also been seen in one case. There is a similarity

* Submitted for publication, May 1, 1929.

* From the Johns Hopkins University School of Medicine.

1. Wertheimer, F. I., and Hesketh, F. E.: Observations and Remarks on the Physical Constitution of Female Psychiatric Patients, Am. J. Psychiat. **6**:499, 1927.

2. Wertheimer and Hesketh (footnote 1). Sprunt, T. P.: Lipomatosis, in Nelson: Loose Leaf Medicine, New York, Thomas Nelson & Son, 1920, vol. 3, p. 199.

between these forms of bodily habitus, with pronounced contrast in fat distribution of the upper and lower parts of the body, and that found in the disease called lipodystrophia progressiva, which has also been designated as "lipomatosis atrophicans."[3] This clinical condition, the etiology of which is unknown, apparently appears in varying degrees.[4] It is usually progressive, but Sprunt[5] described a form in which, under the administration of pituitary extract combined with a high caloric diet, the factors producing the atrophy of subcutaneous fat tissue did not remain active. While the weight of the patient remained constant, the previously emaciated parts gained in volume.

Marañon and Soler[6] claimed that lipodystrophia progressiva in women represents mainly a stressing of the morphologic expression of the secondary sex characteristics. This opinion seems to be contradicted by clinical observations. There are transitions from forms of lipodystrophy to the more frequently found disproportions in the deposition of subcutaneous fat as discussed by Parkes Weber[7] and Bauer.[8] It may be assumed that body forms with pronounced obesity below the waistline combined with marked thinness of the upper part of the body[9] are allied to the clinical syndrome known as lipodystrophia progressiva. For this reason, the term habitus lipodystrophicus has been suggested for these body types.

REPORT OF CASE

Clinical History.—A young woman, aged 22, was of a sociable, cheerful disposition, was inclined to be talkative, and showed a tendency to associate with older people. She developed a strong attachment to an older woman who was her music teacher. About two months before admission to the hospital, she became

3. Günther, H.: Die Lipomatosis, Jena, Gustave Fischer, 1920.

4. Boissonas, L.: La lipodystrophie progressive, Rev. neurol. **35**:721, 1929. Smith, H. L.: Lipodystrophia Progressiva with Report of a Case, Bull. Johns Hopkins Hosp. **32**:344, 1921. Watson, W. N. B., and Ritchie, W. T.: Progressive Lipodystrophy, Quart. J. Med. **18**:224, 1925. Ziegler, L. H.: Lipodystrophies: Report of Seven Cases, Brain **51**:147, 1928. Ziegler, L. H., and Prout, C. T.: Neuropsychiatric Aspects of Lipodystrophic Disturbances, Am. J. Psychiat. **7**:709, 1928.

5. Sprunt, T. H.: Lipodystrophia Progressiva: A Report of Two Cases, One of which Showed Improvement under Medical Treatment, South. M. J. **16**:333, 1923.

Marañon, G., and Soler, J. B.: Progressive Lipodystrophy and Hyperthyroidism, Endocrinology **10**:1, 1926.

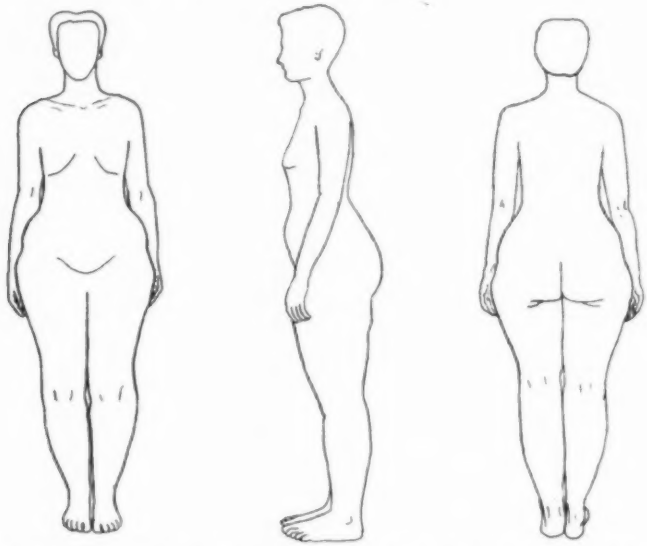
7. Weber, F. Parkes: Lipodystrophia Progressiva, Quart. J. Med. **10**:131, 1916-1917.

8. Bauer, J.: Ueber Fettansatz, Klin. Wchnschr. **1**:1977, 1922.

9. Cases of this type have to be distinguished morphologically from the so-called "segmental obesity" of which Laignel-Lavastine and Viard (Adipose segmentaire des membres inferieurs, Nouv. iconog. de la Salpêtrière **25**:473, 1912) have described a typical case. In this condition, the fat deposition affects only the legs and not the whole body below the waistline.

restless and overtalkative, and wrote disconnected letters. She was intensely preoccupied with her friendship for the teacher and talked at length on this topic. The family history showed one paternal relative who had a mild depression.

In the clinic, the patient showed a tendency to jump from one topic to another in conversation, occasionally suggesting flight of ideas. She was in an elated mood, with feelings of power and energy, and did not understand why she was considered ill. At times she had outbursts of irritability. She was inclined to be extravagant. She made occasional fantastic statements, but in settings of amusement. She gained in weight throughout her stay in the clinic. After about two months, she began to improve and was able to concentrate, read and write coherent letters. She also developed insight into the abnormality of her previous behavior and made consistent plans for her future. After a stay of about four months in the clinic, she was discharged as well.



Drawings (from photographs) illustrating habitus lipodystrophicus in a woman, aged 22, with affective psychosis (hypomanic excitement).

Physical examination on admission showed a blood pressure of 104 systolic; 80 diastolic. The thyroid was palpable, a little firm and not large.

Morphologic Habitus.—The morphologic habitus of the patient was characteristic, as shown in the accompanying illustration. She was well developed, and had a fresh complexion. The difference between the fat of the lower and of the upper parts of the body was striking. Below the waist, she was markedly obese. The contour of the muscles and bones of the lower extremities was hidden by the diffuse accumulation of subcutaneous fat. The fat deposition around the hips and in the gluteal and trochanteric regions was pronounced. In marked contrast to this, the upper part of the body had little subcutaneous fat. The breasts were small and pendulous, with glandular substance but no fat deposition. The face was thin but did not show emaciation. The neck, though of medium length, appeared longer on account of its thinness. The contrast between the thickness of the legs and the thinness of the arms was especially striking.

From observation alone, it was not possible to arrive at a conclusion as to whether the patient could be included in any of the morphologic types of Kretschmer. The results of the anthropometric examination are shown in the table.

Comment.—According to the trunk volume-limb length index, the patient falls within the upper limit of the pyknic type, but near the range of values found in measurements in cases which belonged to neither the pyknic nor the asthenic group (index values from 312 to 346).

The psychosis of the patient shows all the essential features of a mild manic (hypomanic) excitement of affective (manic-depressive) type. Her habitus, if indeed the characteristic distribution of subcutaneous fat can be regarded as a predominant characteristic, was of the lipodystrophic type. According to her skeletal development, she can be assigned to the pyknic or pyknoid group.

Results of Anthropometric Examination

Stature	159.1 cm.
Leg length	90. "
Malleolus height	6.6 "
Transverse chest diameter	27.5 "
Sagittal chest diameter	18. "
Trunk height	53. "
Biacromial diameter	36. "
Bi-iliac diameter	28.5 "
Subcostal angle	70 degrees

Indexes: 1. $$\frac{\text{Leg length} \times 10^2}{\text{Transverse Chest Diameter} \times \text{Sagittal Chest Diameter} \times \text{Trunk Height}} \times 100 = 309$$

2. $$\frac{\text{Bi-iliac Diameter}}{\text{Biacromial Diameter}} \times 100 = 79.2$$

3. $$\frac{\text{Trunk Height}}{\text{Leg Length}} \times 100 = 58.9$$

The incidence of a psychotic condition in association with habitus lipodystrophicus is of interest, especially if it is assumed that there is a constitutional connection between the lipodystrophic habitus and the clinical syndrome, lipodystrophia progressiva. The etiology of progressive lipodystrophy is as yet entirely unclear.[10] In this condition, evidence of endocrinopathy is frequently present; but such different glands have been found affected that there is no foundation for a specific endocrine etiology. A constitutional pathogenic factor seems to be probable.

In the case described, the association with manic-depressive psychosis is of particular interest because in this psychiatric condition, especially in manic excitements, marked disorders in growth of any kind are

10. Oswald, A.: Die verschiedenen Formen der endokrinen und zerebralen Fettsucht, Schweiz. med. Wchnschr. **6**:1048, 1925.

infrequent. In a group of 16 manic patients forming part of an unselected series of 923 psychiatric patients, no growth disorders were found.[11] The association of a marked growth disorder with a manic psychosis is therefore of interest. This observation raises the problem as to whether habitus lipodystrophicus belongs to the group of growth disorders in the sense of Kretschmer's dysplastic signs. It is possible that this habitus may change in the course of growth and development. No studies concerning this subject are as yet available. An anthropometric investigation of the skeletal morphology of the different groups of lipodystrophy and allied conditions would be desirable, as it might throw light on the possibility of biologic relationships.

11. Wertham, F. I.: The Incidence of Growth Disorders in Nine Hundred and Twenty-Three Cases of Mental Disease, Arch. Neurol. & Psychiat. **21**:1128 (May) 1929.

PSYCHOGALVANIC STUDIES ON AFFECTIVE VARIATIONS IN THE MENTALLY DISEASED*

EDWARD M. WESTBURGH
PHILADELPHIA

In our experiments with the galvanometer, my colleagues and I have obtained records on a sufficiently large number of subjects to draw at least tentative conclusions and note tendencies and difficulties which may be suggestive to other experimenters. A number of papers [1] have been published calling attention to differences in galvanic phenomena produced by patients with several types of mental defects. These studies are largely concerned with the variations in resistance to an external electric current or qualitative differences in galvanic deflections. Our work is largely concerned with the quantitative measurement of galvanic responses.

Instead of attempting to demonstrate the effectiveness of the galvanometer for the measurement of emotions, as was done in a previous paper,[2] we are now interested in a comparison of the difference in affectivity of classified patients and normal subjects, and a study of individual patients and individual records.

TECHNIC

The apparatus consists of a mirror torsion galvanometer, glass scale, electric bulb and lens, Ayrton shunt, Wheatstone bridge, one dry cell, nonpolarizable electrodes (liquid) and a stopwatch.[3]

The procedure is briefly as follows: Before the subject is seated in the chair to which the electrodes are attached, his finger temperature is taken and the temperature of the room and the solution of zinc sulphate (electrodes) recorded. Then the subject is seated and the experimenter reads the instructions to him, while the assistant darkens the room and prepares the record blank.

For the patients, the instructions are: "We want you to help us make a little test to see how much better you are. There is nothing here to hurt you and it will take but a short time. All you must do is to put the first finger of each hand (index finger) in the holes (indicating holes in arms of chair) so that the tips of your fingers touch the bottom of the jars.

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* Submitted for publication, March 20, 1929.

* From the Psychological Laboratory of the Department for Mental and Nervous Diseases of the Pennsylvania Hospital.

1. A review of the important papers published and bibliography are given in the Psychological Bulletin **26**:64, 1929.

2. Westburgh, E. M.: Psychogalvanic Studies of Normal Subjects: For the Purpose of Determining the Reliability of the Galvanometer in Investigating the Emotions, Arch. Neurol. & Psychiat., to be published.

"After you have your fingers in the water, I shall say a number of words, about one minute apart. After each word you answer with the first word or thought that comes to your mind, whether it makes sense or not, and do not move or take out your fingers until I tell you to do so. Now, make yourself as comfortable as you can and put your fingers in the holes."

A screen hides the apparatus and experimenter from the subject. The assistant faces the subject and records the deflections of the galvanometer and the subject's verbal responses. After the resistance of the subject is balanced against the Wheatstone bridge, three practice words are given, viz., book, sparrow, walk. Then the stimulus words, mother, grass, stink, chair, murder, corner, woman, tree, spooning, pavement, man, string, home, glass, sex, white, love, stone, kiss, pencil and marry, are given in that order. As is evident, the affective and nonaffective words alternate. In the compilation of results, the stimulus word "man" is not used, leaving ten emotional and ten nonemotional words for comparison. Wherever the concept of mean affective deflection is used, it represents the average galvanic deflection in centimeters for the ten affective stimuli. The mean nonaffective deflection represents in centimeters the average of the galvanic responses to the nonemotional stimuli.

RATING OF MENTAL CONDITION

One feature of the individual study of cases was a clinical appraisal of the patient's mental condition, made by the senior physician (Dr. E. V. Eyman) on each day that a record was taken. At the conclusion of the extended experimentation with each patient, the same physician evaluated the mental condition of the patients on the days that the galvanic records were made.

These evaluations were made on a ten-point scale. Ten represents "N", the normal; 9 might be called "good-plus", or a patient ready for discharge as cured; 8 stands for "good," or a patient to be considered for discharge, though not entirely well; 7 for "good-minus," or a little worse than 8; 6 represents "medium-plus" which is a slight improvement over 5, standing for "medium." ("Medium," as one can readily see, does not mean fairly well, but rather fairly sick mentally.) Four stands for "medium-minus;" 3 for "poor-plus;" 2 for "poor" which means very sick; and 1 for "poor-minus," i.e., as bad as a patient can get. The fact that one physician made all these evaluations, according to the method just described, gives some uniformity to the process. The lack of more perfect controls for these subjective ratings is not as damaging as one might expect before considering the use to which these evaluations are put.

The rating for the first record is the most uncertain, because after that it is easier to judge if the change is up or down. Naturally, a clinical estimate of a subjective type will not show small changes in a patient. Also it is true that because of lack of criteria for what constitutes bad mental health, the clinical observation and the galvanic results may be contradictory. For example, a physician may consider a depressed patient considerably improved if he is displaying increased

vocomotor activity. Similarly, one may believe a patient improved because there is less clouding of consciousness, but who can be certain that the total mental condition is improved?

If the affective life plays an essential part in the health of human beings, may it not be possible that psychogalvanic records of affective changes will be more reliable indexes to the mental health of a person than clinical observations? Our results throw some light on this question, as well as showing significant differences between the classified groups of patients.

RESULTS

The hand temperatures (table 1) of the classified subjects show no significant differences. There is one observation we made which should

TABLE 1.—*Hand Temperature and Resistance of All Classified Groups*

	Hand Temperature		
	Beginning	End	Resistance
Dementia Praecox—23 cases (3 catatonics included)			
Maximum	37.1	35.6	90,000
Minimum	32.0	23.0	15,620
Mean	30	30.0	35,689
Catatonic Dementia Praecox—3 cases			
Maximum	35.6	35.0	90,000
Minimum	24.0	24.5	25,000
Mean	31.0	31.0	46,466
Manic-Depressive, Manic—11 cases			
Maximum	37.2	35.0	52,000
Minimum	24.5	27.0	16,000
Mean	30.0	32.0	31,516
Manic-Depressive, Depressed—6 cases			
Maximum	35.0	35.0	69,000
Minimum	25.0	25.0	17,000
Mean	31.0	31.5	37,392
Paresis—4 cases			
Maximum	34.4	33.9	48,000
Minimum	29.0	29.0	22,000
Mean	31.5	32.0	33,852
Normal—7 cases			
Maximum	33.9	35.0	70,000
Minimum	27.5	25.0	28,000
Mean	31.9	31.0	40,470

be noted, viz., that some subjects with dementia praecox (not more than half of them) had too low hand temperatures for proper balancing of the apparatus, and, therefore, to warm them had to rub their hands or hold lightly an electric bulb. After that the resistance was no longer abnormally high and the apparatus could be balanced.

A comparison of the resistances (table 1) for the various groups discloses nothing of special importance. Although the dementia praecox group contains the maximum resistance found, it also has the minimum. There is only one fact worth noting in connection with resistance, viz., that in general there are no significant differences in resistance between the various groups of patients, except possibly in the case of the patients with catatonic dementia praecox, whose mean resistance is higher than that of any other group, including the "normal." The figures of the dementia praecox group include the subjects with catatonic dementia

praecox who are also given as a separate group. Based on nineteen records of three subjects with catatonic dementia praecox, our general observation is that in profound catatonic stupor the resistance is usually higher than in other psychotic conditions, but in mild catatonic stupor the variations in resistance approximate normal subjects and other patients.

Practically, there are no differences between the various groups in the matter of temperature of the zinc sulphate solution and room temperatures. The time consumed in taking a record ranged from 5 to 35 minutes. The mean times are 10.4 minutes for normal persons, 10.5 for patients with dementia praecox, 10.6 for manic patients, 13.1 for depressed patients and 9.7 for paretic patients.

All the groups of patients show a mean galvanic deflection of double or more for the affective words over the nonaffective words. The

TABLE 2.—*The Mean Galvanic Deflections for Affective and Nonaffective Stimuli of Classified Groups*

	Test Arrangement *			
	Mean (Noncorrected)		Mean (Corrected)	
	Affective	Nonaffective	Affective	Nonaffective
Dementia praecox (23 cases)	2.28	1.08	7.22	3.63
Manic-depressive manic (11 cases)	3.59	1.86	10.77	5.19
Manic-depressive depressed (6 cases)	4.85	2.38	14.21	6.90
Manic-depressive manic and manic-depressive depressed	4.17	2.12	12.49	6.04
Paresis (4 cases)	0.78	0.13	2.90	0.47
Normal (2nd series) (6 cases)	5.36	2.08	18.42	6.90

* Whenever the term "test arrangement" is used it means that the results given are based on the arrangement used by the experimenter, viz., ten stimulus words selected as affective stimuli and ten stimulus words selected as nonaffective stimuli.

dementia praecox group (twenty-three cases) gave a corrected mean[3] deflection of 7.22 cm. for the emotional and 3.63 cm. for the nonemotional words; the manic group (eleven cases), emotional words 10.77 cm., nonemotional 5.19 cm.; the depressed group (six cases), emotional 14.21 cm., nonemotional 6.9 cm.; the paretic group (four cases), emotional 2.9 cm., nonemotional 0.47 cm.; normal subjects (thirteen cases, first and second series), emotional 23.14 cm., nonemotional 10.85 cm. (table 2 and chart 1). Table 2 and chart 1 show a much greater mean deflection for normal subjects than for mentally defective patients. The depressed patients show the next largest deflections; the manic

3. The corrected mean is obtained by multiplying the average deflection for the ten affective and ten nonaffective words of each record for each patient by the resistance and then dividing the result by 10,000. The division by 10,000 is made to reduce the size of the numerals involved. For an explanation of the reason of such corrections, see Wechsler: The Measurement of Emotional Reactions, Arch. Psychol., January, 1925, no. 76.

patients came next, then those with dementia praecox, and the paretic patients last. This is an indication to the effect that the galvanic responses are less in the mentally diseased than in normal people. In fact, the individual records, discussed later, suggest rather forcefully that the psychogalvanic reflexes decrease as the mental condition becomes worse. Furthermore, normal subjects show emotional adaptation (decrease in deflections) on repetition of the same stimuli in successive weeks. Patients, on the other hand, have increased or decreased deflections depending on their health.

Relative to the specific stimuli used, it is interesting to note that the manic patients (chart 2) did not respond affectively to the word "stink"

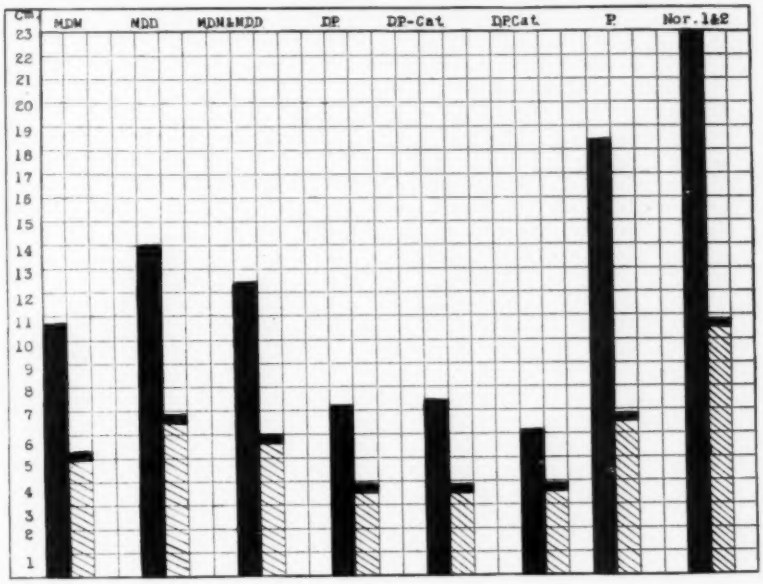

Chart 1.—The mean galvanic deflection for ten affective and ten nonaffective stimuli of the classified groups. The solid column represents the affective stimuli; the striped column, the nonaffective. *M.D.M.* represents the manic-depressive manic group (N, eleven cases); *M.D.D.*, manic-depressive depressed group (N, six cases); *D.P.*, dementia praecox group (N, twenty-three cases); *D.P.-Cat.*, dementia praecox minus catatonic group (N, twenty cases); *D.P.Cat.*, dementia praecox catatonic group (N, three cases); *P.*, paretic group, (N, four cases), and *Nor. 1 & 2*, normal first and second series (N, thirteen cases).

whereas all the other groups did. Manic and depressed patients (charts 2 and 3 and table 3) gave the impression of having large deflections for "glass," but that is only apparent and not real. In the manic-depressive group, two patients [2] were responsible for the inconsistency. They had built up strong emotional associations around a stimulus that is ordina-

TABLE 3.—*Rank Order of Stimulus Words According to the Mean Galvanic Deflection for Each*

	Normal			Manic-Depressive Manic			Manic-Depressive Depressed			Dementia Praecox			Paresis		
Rank Order	Order of Presentation	Word	Mean Galvanic Deflection	Order of Presentation	Word	Mean Galvanic Deflection	Order of Presentation	Word	Mean Galvanic Deflection	Order of Presentation	Word	Mean Galvanic Deflection	Order of Presentation	Word	Mean Galvanic Deflection
1	21	Marry.....	7.28	19	Kiss.....	4.97	15	Sex.....	6.23	19	Kiss.....	2.87	3	Stink.....	1.27
2	15	Sex.....	6.30	15	Sex.....	4.58	17	Love.....	5.85	9	Spooning..	2.70	1	Mother.....	1.13
3	9	Spooning..	6.23	1	Mother.....	4.52	9	Spooning..	5.36	15	Sex.....	2.51	5	Murder.....	1.50
4	1	Mother.....	5.19	17	Love.....	3.81	5	Murder.....	5.23	1	Mother.....	2.45	11	Man.....	1.00
5	19	Kiss.....	5.12	9	Spooning..	3.50	19	Kiss.....	5.22	7	Woman....	2.02	21	Marry.....	0.87
6	13	Home.....	5.07	5	Murder.....	3.09	14	Glass.....	4.96	13	Home.....	1.92	9	Spooning..	0.75
7	17	Love.....	5.01	14	Glass.....	3.05	21	Marry.....	4.92	17	Love.....	1.90	13	Home.....	0.62
8	3	Stink.....	4.71	7	Woman....	2.87	7	Woman....	4.65	2	Grass.....	1.63	15	Sex.....	0.52
9	5	Murder.....	3.37	21	Marry.....	2.86	1	Mother.....	4.62	3	Stink.....	1.56	17	Love.....	0.50
10	11	Man.....	3.30	13	Home.....	2.65	3	Stink.....	4.39	21	Marry.....	1.56	19	Kiss.....	0.50
11	7	Woman....	3.00	4	Chair.....	2.31	11	Man.....	4.24	5	Murder.....	1.51	6	Corner.....	0.31
12	16	White.....	2.70	2	Grass.....	2.04	10	White.....	3.84	6	Corner.....	1.45	7	Woman....	0.31
13	2	Grass.....	2.62	6	Corner.....	1.98	2	Grass.....	3.29	4	Chair.....	1.35	14	Glass.....	0.31
14	6	Corner.....	2.42	3	Stink.....	1.92	6	Corner.....	2.79	8	Tree.....	1.30	16	White.....	0.22
15	8	Tree.....	2.36	12	String.....	1.90	13	Home.....	2.76	11	Man.....	1.26	18	Stone.....	0.20
16	12	String.....	2.20	16	White.....	1.70	4	Chair.....	2.43	12	String.....	1.25	4	Chair.....	0.12
17	4	Chair.....	2.03	18	Stone.....	1.56	18	Stone.....	2.39	14	Glass.....	1.23	20	Pencil.....	0.07
18	10	Pavement..	1.87	11	Man.....	1.51	10	Pavement..	2.13	18	Stone.....	0.87	8	Tree.....	0.06
19	18	Stone.....	1.70	8	Tree.....	1.45	8	Tree.....	1.77	10	Pavement..	0.81	12	String.....	0.06
20	14	Glass.....	1.37	10	Pavement..	1.41	12	String.....	1.55	20	Pencil.....	0.80	2	Grass.....	0.00
21	20	Pencil.....	1.37	20	Pencil.....	1.15	21	Pencil.....	1.20	21	White.....	0.69	10	Pavement..	0.00

rily nonaffective. These two cases emphasize the necessity of studying each response of each record separately for every subject. Individual persons will have emotional associations with situations that are ordinarily nonemotional. The former, as well as many less striking illustra-

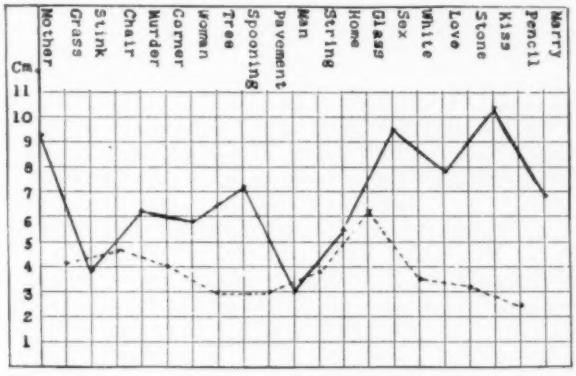

Chart 2.—The mean galvanic deflection for each stimulus word for manic-depressive manic patients. The solid line represents the affective stimuli; the broken line, the nonaffective stimuli. In this chart and charts 3, 4, 5 and 6, reading the stimulus words from left to right indicates their order of presentation.

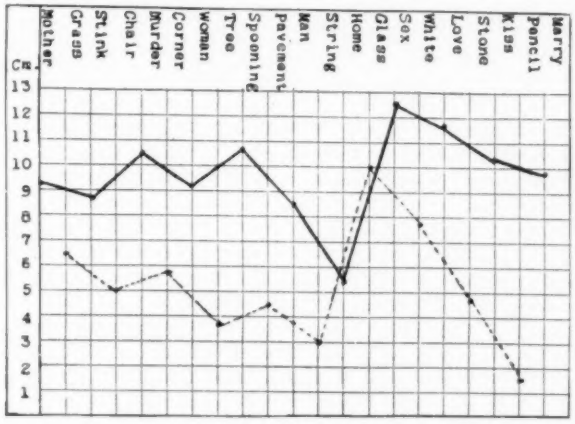

Chart 3.—The mean galvanic deflection for each stimulus word for manic-depressive depressed patients. The solid line represents the affective stimuli; the broken line, the nonaffective stimuli.

tions, could be given and they all suggest that stimuli selected on their relationship to the more pronounced experiences of the patients may show which of those experiences have done the greatest harm and around which "complexes" have been built.

Returning to charts showing results of specific stimuli, it will be noted that persons with dementia praecox and paretic and normal persons (charts 4, 5 and 6) show no overlapping for the individual affective and nonaffective words. These charts, and also the former two, give added support to those who believe that the galvanometer measures differences in affect. Table 2 illustrates the same point.

COMMENT

The comment on individual cases may well be introduced by considering the magnitude of deflections of the first five patients in several of the groups of whom records were taken (chart 7).

Although the ten cases are given merely as examples, they (especially if all the cases are considered) create a strong conviction that manic and depressed patients give little or practically no deflections when they are very manic or very depressed, and that the magnitude of the deflection increases as they become less manic and less depressed. If the means of the half of the records representing the period of greatest illness were compared with the means of the records representing the improved condition, the magnitude of the latter would be much greater than that of the former. This phenomenon cannot be explained on the basis of lack of attention alone. Attention may be a factor, but the truth is that the greater number of the records covering the periods when the patients were most ill show logical word associations for the stimulus words. Furthermore, if these patients were not attentive to the stimuli given, they should be reacting to internal mental stimuli or irrelevant external stimuli, which would indicate their presence by sudden deflections or constant fluctuations of the galvanometer. This is rarely so and when it happens it indicates that a few experiences still do have affective meanings. This is supported by the fact that most of these patients will give one or two very large deflections for some one or two of the regular stimulus words. In such instances, the large deflections are related to some intense experience; for example, a patient always asking to go home gave a large galvanic response to the word "home"; a patient bitter against his mother gave a large deflection to that word; the patient previously referred to and described in an earlier paper gave a large deflection to "glass."

Our observations lend support to the belief that manic and depressed patients have decreased affect. The euphoric and melancholic patient is probably not happy nor sad, but merely displays the verbal and motor responses appropriate to those moods or affects. The emotions may be blocked or may be temporarily inoperative, while the vocomotor responses continue to function.

Chart *7b* is interesting when compared with chart *7a*. The five patients with dementia praecox illustrate the usual results given by

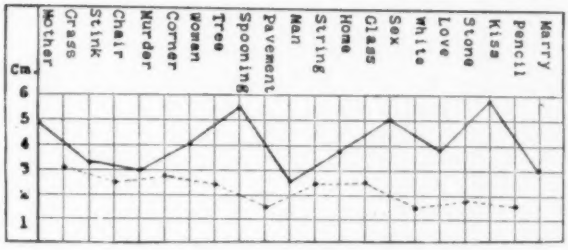

Chart 4.—The mean galvanic deflection for each stimulus word for patients with dementia praecox. The solid line represents the affective stimuli; the broken line, the nonaffective stimuli.

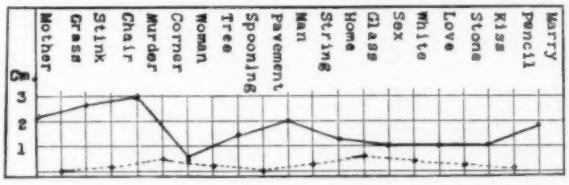

Chart 5.—The mean galvanic deflection for each stimulus word for patients with paresis. The solid line represents the affective stimuli; the broken line, the nonaffective stimuli.

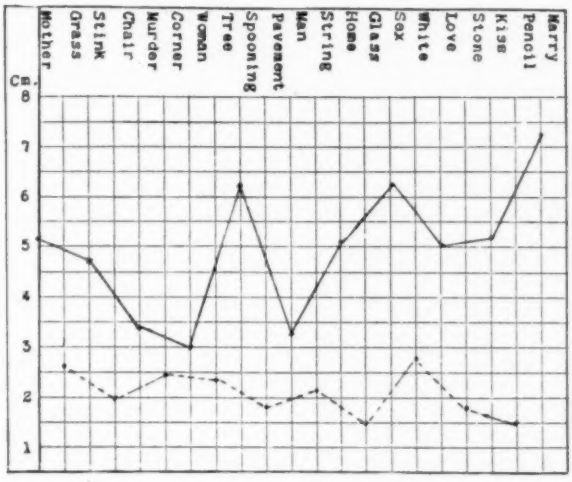

Chart 6.—The mean galvanic deflection for each stimulus word for normal subjects. The solid line represents the affective stimuli; the broken line, the nonaffective stimuli.

patients with dementia praecox. Apparently, their affectivity is reduced in a uniform manner. The galvanic responses are similar to the galvanic responses of normal subjects in quality, but reduced in quantity. Normal subjects give larger galvanic deflections than mentally defective patients. The two subjects shown in chart *7a*, who were almost well, approximate the normal subjects.

The charts that follow are all of individual cases, plotted on the basis of the total affectivity (the sum of the corrected mean deflection for the ten affected words and the corrected mean deflection for the ten nonaffected words) and the clinical rating of the physician. Chart 8 shows two patients with dementia praecox whose illnesses had not

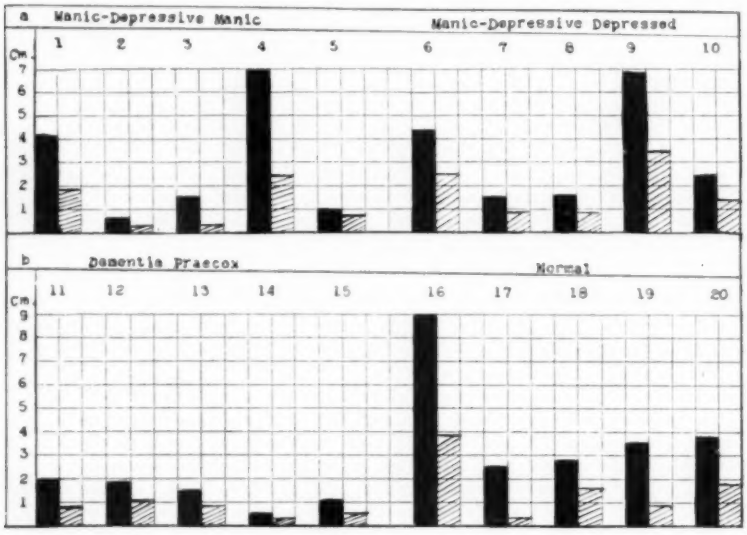

Chart 7.—Mean galvanic deflection for affective and nonaffective stimuli for the first five subjects of several classified groups: *a*, manic-depressive manic and manic-depressive depressed patients; *b*, patient with dementia praecox and normal subjects. The solid block represents the affective stimuli; the striped block, the nonaffective stimuli. Double column *1* represents a hypomanic patient who was practically well when two of the records were taken; *2*, an extremely manic patient who was transferred to another hospital without showing any change here; *3*, an extremely manic patient who recovered suddenly (his last record alone covered an improved state); *4*, a mildly hypomanic patient who was almost well when most of the records were taken; *5*, a patient strongly manic over most of the period included in the chart; *6*, a patient in a deep depression who gave very little deflections while in depression and gave very large ones when he came out of the depression; *7*, a patient uniformly depressed over a period of four months; *8*, a patient who was depressed most of the time, with some improvement toward the end; *9*, a patient who had already come out of a profound depression and was only mildly depressed when the first record was taken, and *10*, a patient mildly depressed, who showed some improvement toward the end.

been of long duration. These indicate the general trend of newer cases in the sense that patients with earlier cases of dementia praecox are apt to display more affectivity than those with older ones.

Chart 9 shows the total deflections (weekly) of more deteriorated cases. Of the ten patients with dementia praecox whose curves were plotted (only four shown on charts), several seem to show real

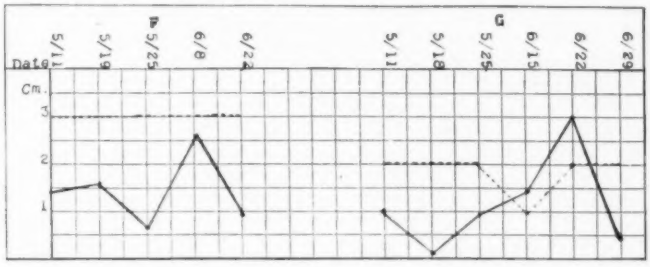

Chart 8.—Comparison of the mean galvanic deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for two patients with dementia praecox, *F* and *G*. In this and the subsequent charts, the solid line represents the mean deflection for twenty stimulus words, or the total affectivity for the days on which records were taken; each square represents 5 units (1 unit equals 1 cm.). The broken line represents the physician's rating for the same days (two squares equal 1 unit). A unit for the galvanic deflections is one tenth of the physician's rating unit. In this and the following charts, when no specific year is given the dates refer to 1927.

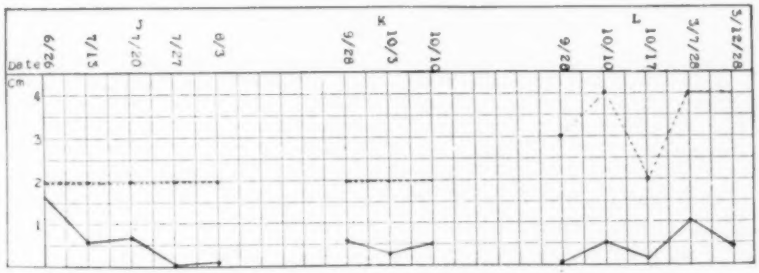

Chart 9.—Comparison of the mean deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for three deteriorated patients with dementia praecox, *J*, *K* and *L*.

agreement between the clinical rating and the galvanic responsiveness. Small variations between the two lines are not actual disagreements when it is realized that the galvanometer unquestionably records smaller changes in the organism than a clinical observation can disclose, and that each line for the galvanic deflection shows fine changes with each

block representing 5 cm., while the health line is constructed on a ten-point scale, with each two blocks representing one point.

When studying these and subsequent charts, it is also well to keep in mind that the record of the first week may show a greater total affectivity than is normal in comparison with the succeeding records. In the laboratory, some subjects display increased emotional excitation

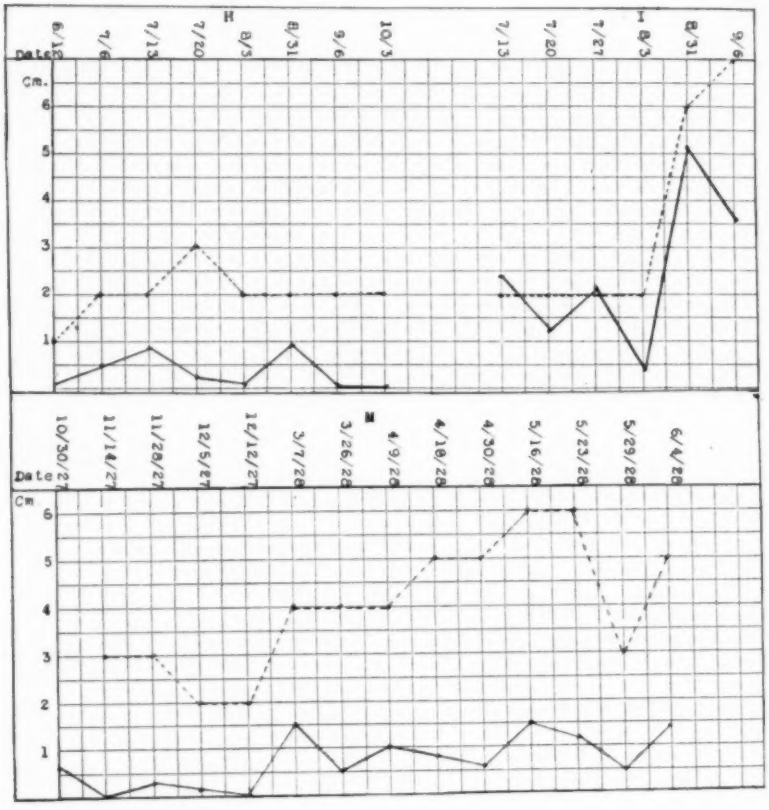

Chart 10.—Comparison of the mean deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for three catatonic patients, *H*, *I* and *M*.

during the first sitting because of the strangeness of the apparatus and procedure. Also one should not forget that a decrease in deflections frequently occurs when a patient is almost well because of emotional habituation to those stimuli which have been repeated throughout the whole experiment.

Chart 10 represents patients with catatonic dementia praecox. There was little change in case H during the course of the experiment, while

in cases I and M [4] there was considerable change. The patient in case I improved sufficiently to be discharged and the patient in case M became worse and then improved somewhat. The agreement between the clinical and the galvanic line is rather marked.

Three of the four paretic [5] patients of whom records were taken gave startling results (chart 11). The fourth patient is not included because his record was not completed. He was removed from the hospital before a postmalarial record could be taken. The three patients who improved had a rise in deflections from zero or near it before the malarial treatment, to 3.7, 13.3 and 12.2 cm., respectively, after the chills.

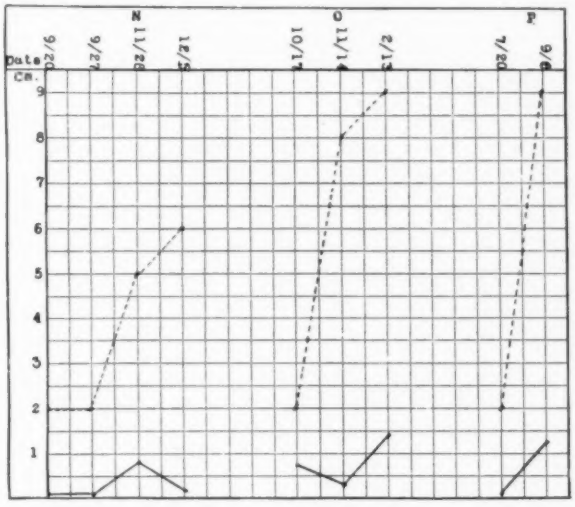

Chart 11.—Comparison of the mean deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for three paretic patients, *N*, *O* and *P*.

4. The records in case *M*, chart 10, involve some changes in apparatus which were made between March 7, 1928, and the previous record. As an improvement, new arm rests were made to provide more comfortable positions for the hands and fingers, and an arrangement was attached for keeping the zinc sulphate solution at a uniform temperature. The straight part of two curling irons is stuck in an asbestos pocket under the glass jar containing the water in which the receptacle with the zinc sulphate is placed. There are two openings in the top layer of asbestos which allow the heat to get to the glass jars. If one or both solutions get too hot, the curling irons can be pulled out so that they are under only one of the holes, or the heat can be turned off altogether. In order to be able to make the proper adjustments of the heating arrangement, a thermometer remains constantly in each jar of water. In this way it is possible to keep the zinc sulphate solution at an almost constant temperature.

5. Records were taken only of paretic patients who had been selected for malarial treatment. One or more records were taken before the treatment and then one or more after the fever had passed.

Several cases of depressed patients on charts 12 and 13 show remarkable agreement between the health line and the galvanic responses. In the curves of six of the nine manic patients which were plotted (only two shown in chart 14,) the health line and the galvanic line run fairly parallel. One of these, case T, is really remarkable. The patient had been manic before a galvanic study of him was begun and then he recovered, but continued at the hospital for many months in order to have medical attention available if another attack started. While well, his deflections were so uniformly normal, according to what has come to be regarded as normal, that no more records were taken until he began to become manic again. He showed a remarkable drop from 33.16 cm. total mean affectivity, to a mean of 3.67 cm. The experiment could not

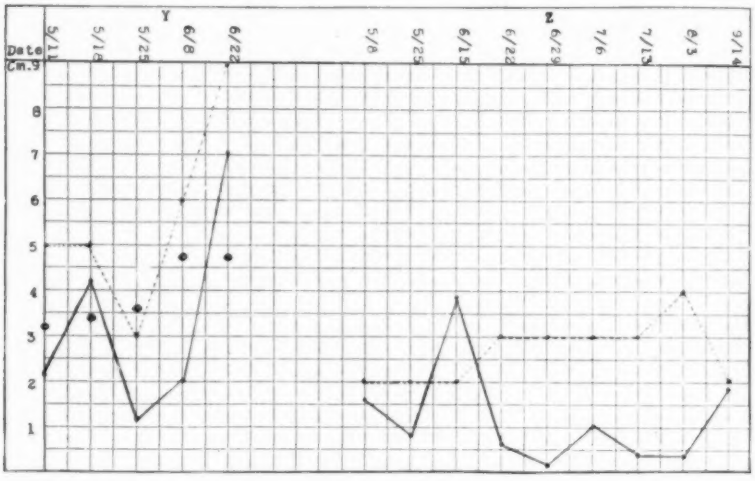

Chart 12.—Comparison of the mean deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for two depressed patients, *Y* and *Z*. In this and the following charts, the circles represent the galvanic resistance for each record; each square represents 5,000 ohms.

be continued because he did not remain at the hospital. It is also significant that this patient apparently gave good attention to the stimulus words as evidenced by his logical and meaningful word associations to the stimuli. This case is unique in that records were obtained from him as a normal subject and then followed with two records as he grew manic.

Another most satisfactory record is case Y, chart 12. This was a case of real depression showing some variations and then a complete recovery. Further, the agreement between the health and galvanic lines is remarkable. This patient gave sensible word responses to the stimuli while he was in a depression. In both these cases the changes in resis-

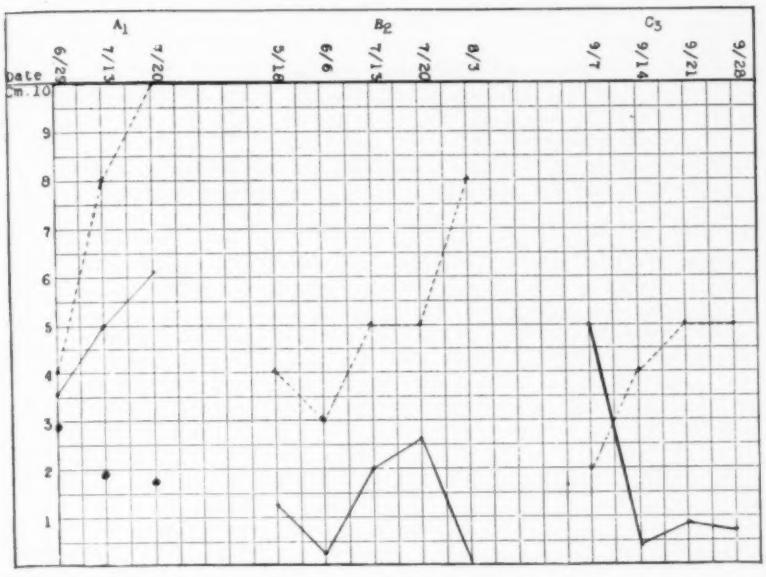

Chart 13.—Comparison of the mean deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for three additional depressed patients, A_1, B_2 and C_3.

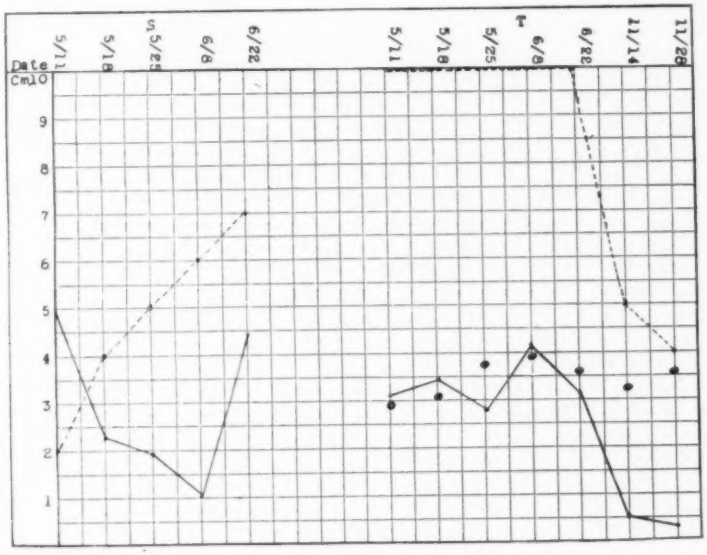

Chart 14.—Comparison of the mean deflection for twenty stimulus words, with a physician's rating on a ten-point scale, for two manic patients, *S* and *T*.

tance do not account for the pronounced decrease and increase in galvanic deflections.

As stated in the first paper from this laboratory on psychogalvanic studies, large increases in resistance of from 30,000 to 60,000 ohms produce a decrease in galvanic deflections, and if there is a marked decrease in resistance the galvanic deflections increase. In view of these inverse changes, it would not be difficult to believe that the galvanic deflections may have increased because the resistance decreased, and vice versa, and that this takes place even when the changes in resistance are less than 30,000 ohms. Such a position might be maintained provided the resistance did decrease as the patient became better and increased as the patient became worse.

In both of the cases that are being emphasized, the reverse was true. The patient in case T, chart 14, had a slight decrease in resistance at the onset of the manic attack. The resistance for each record were 28,500, 30,200, 37,700, 38,000 and 36,000 ohms when the subject was normal; then 32,000 and 35,000 ohms during the manic attack. Yet with a small decrease in resistance at the onset of the attack, the galvanic deflection dropped to approximately one sixth of its former magnitude. Case Y, chart 12, instead of showing increased deflections with decreased resistance, displayed very greatly increased deflections with increased resistance as the patient grew better. This patient's resistance started with 32,400 ohms, then increased to 33,200, 36,800, 47,000 and 47,000. The first three resistances were in periods of profound depression, the latter two during marked improvement.

The foregoing comment is not an attempt to prove that normal persons becoming manic show a decrease in resistance, nor is the intent to demonstrate that as a patient comes out of a depression and gets well the resistance increases. The last patient considered behaved in such fashion and so do others, but there are many of whom the reverse holds true. A good illustration is the depressed patient, case A, chart 13. Instead of having increased deflections with increased resistance, this patient had increased deflections with decreased resistance.

What these cases do illustrate is that galvanic deflections increase and decrease irrespective of the usual changes in resistance and that increased galvanic deflections probably indicate increased affectivity and increased affectivity apparently goes with improved mental health and decreased affectivity with decreased mental health.

SUMMARY

1. There are no significant variations in the temperature of the solution and room which could account for the differences in deflections disclosed by the classified mental groups.

2. The differences in hand temperatures between the groups are slight, except in the case of patients with dementia praecox, some of whom had low finger temperatures. In such cases, rubbing or warming the hands eliminated the difference and so gave uniformity to all the group temperatures.

3. The various groups show no significant differences in resistance to the passage of a small electric current except in the cases of patients with profound catatonic dementia praecox, who have increased resistance. As a group, subjects with dementia praecox tend to have smaller resistances than depressed or normal subjects.

4. The groups of mentally defective patients and normal subjects display a relationship between resistance and magnitude of galvanic responses: (*a*) Large changes in resistance which remain reasonably constant (not the brief change in resistance resulting from the stimulus) produce a general change in the magnitude of galvanic response. Large increases in resistance tend to reduce the magnitude of galvanic deflections; large decreases in resistance tend to increase the magnitude of deflection. (*b*) Small changes in resistance of a constant type show no effect on the magnitude of galvanic responses. A change in the constant resistance from 1,000 to 20,000 ohms is considered small.

5. Patients with catatonic dementia praecox give the smallest galvanic deflections. There seems to be an emotional blocking as well as a retardation in thought and motor activity.

6. As a group, patients with dementia praecox apparently have smaller galvanic deflections than other groups. The greater the deterioration, the smaller is the deflection. In newer cases, the galvanic responses are similar to those in normal subjects, from the point of view of uniformity, but reduced in magnitude.

7. The manic-depressive group shows less uniformity in galvanic deflections than patients with dementia praecox and normal subjects and has smaller deflections than normal subjects. There is some indication that depressed subjects display greater affectivity than manic subjects, as measured by the galvanometer.

8. The greater galvanic response of the manic-depressive group over the dementia praecox group is more apparent than real. The mean deflections for the former include, in most cases, records of the patients when they were considerably improved, whereas the dementia praecox group has very few cases which showed improvement. Several subjects with dementia praecox who did improve also showed an increase in galvanic deflections.

9. There is good evidence that pronounced cases of mania and depression give no, or little, deflection, but show a marked increase in galvanic responsiveness as the patients improve in health. Patients

with dementia praecox, and paretic patients treated with malaria, show an increase in magnitude of deflections if they display unmistakable clinical signs of improvement.

CONCLUSIONS

The psychogalvanic measurements show real promise of aiding in diagnosis, suggesting methods of therapy and yielding checks on the effectiveness of therapeutic measures: (*a*) by disclosing differences in quality and magnitude of responses peculiar to the various mental groups; (*b*) by indicating the significant experiences which may have caused or contributed to the psychoses; (*c*) by indicating, a few days or a week before it is clinically observable, that another attack of mania or depression is beginning, or that improvement is taking place, and (*d*) by indicating whether each application of therapeutic measure is having a favorable or unfavorable effect on the patient.

AN APPARATUS FOR THE INDUCTION OF MUSCULAR RELAXATION AND SLEEP*

JOSHUA ROSETT, M.D.†
NEW YORK

The mechanical device to be described was originally intended to answer the following question: What might be the physiologic effect of a wave of circular compression applied to the periphery of the body in the direction of the venous flow? It was hoped that a purely mechanical drive of the contents of the peripheral veins, acting as might a heart for these vessels, would assist in the solution of certain problems connected with the pressure back of them—in the capillary and arterial bed. A discussion of the subject with specialists in that branch of medicine revealed, moreover, the extent to which the profession is in need of information on this point. Experiments with the apparatus in question have been in progress now nearly three years. From both a theoretical and a practical point of view the effects, as will be seen, are sufficiently striking and important to deserve the attention of physiologists and of practitioners in almost every branch of medicine.

THE INSTRUMENT

The instrument, as shown in the illustration, appears somewhat like a union suit. It is made of fine, strong, inelastic, rubberized cloth and is composed of a series of strongly joined flat, beltlike, collapsible tubes which encircle the limbs and the body as high as the line of the armpits.

By means of an air compressor and exhaust, compressed air enters the garment in such a manner that tubes are momentarily inflated and deflated one after another in succession, in a direction from the extremities toward the upper part of the chest and shoulders. The arrangement is such, however, that the successive inflations and deflations are true for any series of adjoining six tubes only, while tubes throughout the garment which belong to the same number in the series of six are inflated and deflated simultaneously. As the exposed parts of the tubes are 2 inches (5 cm.) wide, the result is that the wave of compression is everywhere 12 inches (30.48 cm.) long. This length of the wave was ascertained, after repeated experimentation, as the optimum for the effects to be described.

The degree of pressure exerted by the wave is regulated by a valve in connection with the air compressor. A pressure of a few grams on a square inch of body surface might appear to be too slight for any pronounced effects. It must be remembered, however, that the wave of compression encircles the limbs and the body as might a rubber band and, what may seem to be a slight pressure on a small area of surface becomes considerable when the pressure is an encircling one. It has been found practical to gage the degree of pressure exercised, not by

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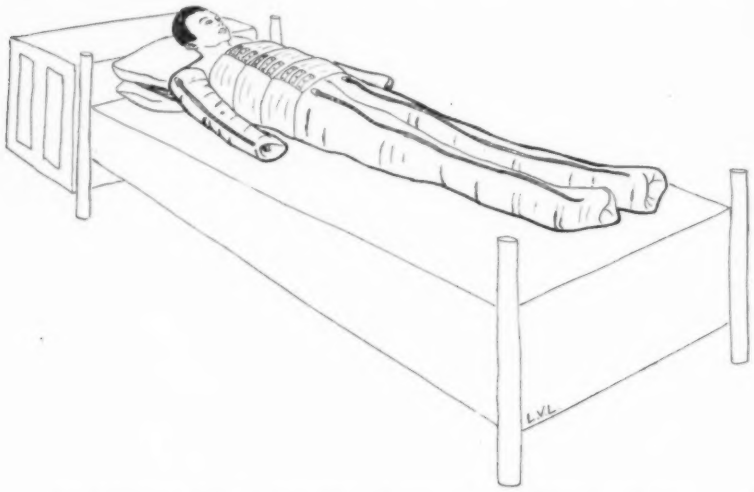
† From the Department of Neurology, Columbia University.

a manometer (which was thoroughly tried and finally discarded as useless) but by the comfort of the person. Persons vary within wide limits in this respect.

The speed of the wave was first regulated by a rheostat attached to a separate electric motor which rotated the distributing device of the air compressor. It was found that at a rate of repetition of the wave of about 15 a minute, the successive inflations and deflations of the encircling tubes were no longer felt by the subject as a wave, and the sensation was no longer agreeable, while the succession of waves at a rate of 30 or more a minute was described by the person as "an unnatural rhythm"—a fact to which I can testify from my own experience. The rheostat and separate motor were finally discarded and a uniform rate of repetition of the wave of 25 a minute has been established as the optimum.

The garment fits persons of all but extraordinary size. The part which envelops the trunk, being made of three flaps and fastened with a series of hooks and eyelets, will fit a thin waist, a protruding abdomen, and hips and chest of



An apparatus for the induction of muscular relaxation and sleep.

almost any size. The parts for the limbs are made to encircle them by hookless fasteners (zippers). By means of a special regulating valve attached to the air intake, a certain quantity of air can be made to remain in the tubes without interfering with the wave action. By means of this residual quantity of air, the limb parts of the pneumatic garment are fitted to limbs of all but extraordinary thickness. The garment is adjusted to a 6 foot length. In the case of taller persons a part of the feet and upper part of the chest remain uncovered; in the case of shorter persons, a part of the garment extends beyond the feet. For sanitary reasons patients were furnished with special underwear before they were placed in the pneumatic garment.

EFFECTS

Sensation.—The instrument has been in operation almost daily, for a number of hours, now nearly three years. It has been tried on hundreds of persons of both sexes and ages between 11 and 75. With the exception of two negativistic neurotic patients, the sensation

experienced has been uniformly declared to be agreeable. Most persons describe it as "a gentle massage all over the body by many fine fingers"; others, as a "pleasant, soothing rhythm"; still others, as a sensation of "floating in the air" or "upon the waves"; others still, as being "soothed to sleep."

Appearance of the Subject.—After thirty minutes' treatment, the appearance of the subject changes in a remarkable way. The gray or purple color of persons suffering from anemia or hypertension disappears, as does the tense, wizened or fatigued expression of the highstrung, the anxious or the hyperactive person. The face becomes young-looking, pink and fresh.

Muscular System.—The uniform effect has been that of relaxation. In from five to fifteen minutes, tense muscles are palpably relaxed. All persons on whom the apparatus was tried were asked how they felt a few minutes after the beginning of the treatment, and the uniform reply has been "very much relaxed." For the experiments, I have picked out from the Vanderbilt Clinic very rigid, postencephalitic parkinsonian patients. In the course of from thirty to forty-five minutes—in a few cases as long as an hour—the rigidity was very much diminished, and in some cases disappeared. The patients came out of the apparatus "limber." They shuffled along before the treatment; they walked in a normal or almost normal manner after it. The same was true of the residual rigidity of hemiplegic persons, in whom, moreover, the diminution of the muscular rigidity was coincident with a corresponding diminution of the exaggerated tendon reflexes. Of course, in these patients the relief was transient. But in the case of the muscular tensions which are part of states of anxiety, of overactivity and particularly of hypertension, the ensuing relaxation lasted many hours, and after a number of treatments became relatively permanent. The patients appear to become conditioned—they acquire the habit of being relaxed. The muscular spasticity consequent on trauma is strikingly relieved. The spasmodic rigidities, on the other hand, such as the rigidity of myotonia congenita, were not influenced by the action of the apparatus.

Nervous System.—The majority of persons fell asleep under the action of the instrument in from five to fifteen minutes, and they slept soundly for thirty minutes or more. A remarkable feature in these experiments has been the fact that at the first two or three trials a number of persons who slept did not know, on awakening, that they had been asleep. A good test was discovered in the person's ability to estimate time. Thus, asked how long he had been in the apparatus, a patient might reply "five or ten minutes"; as a matter of fact, he had been in it from thirty to forty-five minutes. A certain number of such

persons, however, subsequently recollect having dreamed during the first stage of the treatment, and so conclude that they must have slept. During subsequent treatments, however, they are aware, on awakening, of the fact that they have been asleep. Children and very young persons fall asleep with astonishing rapidity. A sturdy boy of 11 whom nothing could ever induce to sleep during the day fell asleep within five minutes in the instrument in a bright light and in the presence of half a dozen people.

From the fact that relaxation and sleep are the most uniform effects of the apparatus, it may be surmised that the threshold to all stimulation is raised, and this surmise is borne out by experimental proof. All sensation is blunted. The patient is for the time being less susceptible to sound, to light, to touch, to pressure and to other forms of external stimulation; the same is true of internal sensation. This will be discussed further in connection with hypertension.

Attention.—The apparatus lends itself well to a study of the mechanism of attention.

Although the wave of compression travels over the entire body and the limbs, it is felt only in one, two or at most three limited areas at a time—in the areas on which attention is directed. Thus a person might say to himself "I don't feel the waves over my knees" and, immediately following this thought, there appears the sensation of the waves over those parts. The same is true of every part.

If the person is not asleep in fifteen minutes or so, the blunting of the sensation is manifested by the fact that the pressure of the waves is felt much less keenly and the mental effort necessary for experiencing it in any one part is greater.

A number of other features pertaining to the same subject must be reserved for a more detailed report.

Circulatory System.—In a number of cases of hypertension, the blood pressure, both systolic and diastolic, gradually falls under the action of the instrument to a certain point in the course of from thirty to forty-five minutes, then remains stationary. The reduction of the blood pressure is greater as the initial pressure is higher. Thus, when the initial pressure is 220 systolic and 130 diastolic, it may fall to about 160 systolic and 110 diastolic; while when the initial pressure is 140 systolic and 100 diastolic, the fall is only to about 130 systolic and 90 diastolic.

This reduction in the blood pressure is largely independent of the fact that the person is resting quietly in the recumbent position. In a number of instances, persons with a blood pressure of about 200 systolic and 120 diastolic were made to lie quietly for half an hour for the purposes of the experiment. By this procedure their blood pressure was seldom reduced more than 15 systolic and 5 diastolic.

They were then placed in the apparatus for half an hour, and when their blood pressure was taken it showed a reduction of many more millimeters of mercury than had been obtained by the preliminary rest.

Regarding the causes of the foregoing phenomena, the following considerations may be of interest:

Concomitant with the muscular relaxation which takes place under the action of the instrument is a state of diminished conductivity of the nervous system. This is evidenced by the state of somnolence and sleep and is easily proved by the ordinary sensory tests. Physiologically, such a state of the nervous system is one of general inhibition. Pavlov's [1] experiments prove this clearly. In a series of experiments on the induction of epileptic seizures in human beings, I have shown the same to be true. It is only reasonable to assume that the muscular relaxation which takes place under the action of the instrument in question is itself a result of the state of nerve inhibition induced. And although the effect of the treatment described on nonstriated musculature has not been studied, it is a reasonable assumption that a general state of nerve inhibition sufficient to cause somnolence and sleep in a few minutes may cause relaxation of certain involuntary as well as of voluntary musculature. And relaxation of the involuntary musculature of the arterioles must result in a diminished pressure in those cases in which the increased pressure is due to a spasm induced by abnormally strong neural impulses. It is perhaps in this class of cases that Mosenthal [2] found relaxation most effective.

REPORT OF ILLUSTRATIVE CASES

Case 1.—An active business man, aged 40, complained of a sense of restlessness, hyposomnia, great susceptibility to the noises of the city and of other symptoms indicative of a general state of hypersensitiveness in the physiologic sense of the word. On examination he appeared to be normal in every way, except for a systolic blood pressure of from 150 to 160 and a diastolic pressure of from 100 to 110. He slept soundly under the action of the apparatus as long as it was operated. At the end of the treatment, his blood pressure was 125 systolic and 90 diastolic. While this patient was being treated, a certain type of air compressor was being tried out which proved to be an exceedingly noisy machine. He declared that the action of the apparatus on him was so quieting that, notwithstanding his great susceptibility to noise, he did not mind in the least the loud rumble directly behind his head.

Case 2.—A married woman, aged 34, of healthy appearance, has been treated for a number of years for "essential" hypertension by means of drugs, vaccines, prolonged rest in bed—indeed by every means known to the medical profession—without any noticeable relief. Her blood pressure, during a moderately active day,

1. Pavlov, J. R.: Conditioned Reflexes, trans. by G. V. Anrep, London, Oxford University Press, Humphrey Milford, 1927.

2. Mosenthal, H. O.: The Treatment of Essential Hypertension, J. A. M. A. **91**:698 (Sept. 8) 1928.

was, on the average, 230 systolic and 130 diastolic. After a rest in bed for a number of days, the systolic pressure dropped to about 190 or 200 and the diastolic to 125 or 120. During the winter of 1927 to 1928, she was treated by means of the apparatus in question for from forty-five to sixty minutes each time. She relaxed profoundly during the treatment, but did not sleep. At the end of each treatment the systolic pressure was from 130 to 160, the diastolic from 100 to 110. By the summer of 1928, after about fifty treatments, her blood pressure was normally about 160 systolic and 110 diastolic. She was not treated during the summer and fall of 1928, but the report of her physician was that the blood pressure remained on the average 160 systolic and 110 diastolic. It rose again in the winter of this year. A treatment given her while the composition of this article was in progress reduced (temporarily of course) the blood pressure from 230 systolic and 130 diastolic to 160 systolic and 100 diastolic. The distance from New York at which this patient lives at present makes further treatment by means of the apparatus in question impracticable for the time being.

It is a certainty, however, that in a large number of cases hypertension is due to permanent changes in the wall of the arterioles. Kernohan [3] has examined the arterioles of skeletal muscle obtained by biopsy from patients with hypertension in the Mayo Clinic, and in a number of cases he has found a remarkable narrowing of the lumen and a thickening of the wall. "In a normal vessel," is the statement, "the ratio of the wall to lumen is 1:2 . . . in hypertension there is a definite upset of the ratio. There is hypertrophy of the media. There is a varying hypertrophy of the internal elastic lamina. Occasionally, there is endothelial proliferation of the intima . . ." As the skeletal musculature constitutes about one third of the bulk of the body, such a narrowing of the lumen of the walls of its arterioles must give rise to a pronounced increase of the resistance offered to the passage of the fluid through them. In such cases an inhibition of the nerve impulses acting on the musculature of the arterioles would be productive of little or no effect. This may be the reason why the treatment in question, although effective in the production of muscular relaxation and sleep is, as will be seen, in certain cases inadequate to reduce hypertension. The two following cases illustrate this point:

CASES 3 and 4.—Two patients, women, aged about 58, of the high-strung, anxious type, underweight, with a hemoglobin index of 70 and 75, and a blood pressure of 160 systolic and 100 diastolic and 170 systolic and 110 diastolic respectively, relaxed under the action of the apparatus in a pronounced way. Nearly every time they fell asleep within ten minutes, and on a number of occasions one of them slept for twenty minutes after the treatment was discontinued. After each treatment, they felt rested and refreshed. After a number of treatments, they both benefited in a number of ways. They gained weight. They slept well

3. Anderson, E. W.; Kernohan, J. W., and Keith, N. M.: Histologic Studies of the Peripheral Arterioles in Ambulatory Patients with High Blood Pressure, Proc. Staff Meetings Mayo Clinic **3**:314 (Oct. 31) 1928.

at night. The sense of being hurried and driven—"living under pressure" as one of them expressed it—passed away, and they could engage in their daily duties or pleasures in a complacent and systematic manner. During the treatments, their blood pressure seldom dropped a few points.

Physicians are familiar with the fact that in certain patients the hypertension can be reduced by various means at certain times with much greater ease than at other times. In the course of the experiments on hypertension with the apparatus described, the same was found to be true, notwithstanding the fact that the patient relaxed, perhaps slept as well when the hypertension was reduced a little as when it was reduced much. Since the inhibitory effect on the nervous system was the same in both instances in the same patient, the hypertension itself could not be due to a spasm of the arterioles induced by supernormal neural impulses; since the hypertension in these cases was of the reducible kind, it could not be due to any extensive pathologic change in the walls of the vessels. It must have been due, therefore, to a contraction of the musculature of the vessel wall brought about, not by nerve impulses, but directly, perhaps as the result of the occasional presence of certain substances in the blood the action of which is immediately on the muscular tissue.

A fourth class of cases was encountered in these experiments, exemplified by the following:

Case 5.—A woman, aged 60, complained of severe attacks of pain and pulsation in the head and ringing in the ears. She had cataract in both eyes, one of which was operated on without success. A retinal hemorrhage in one eye took place four months before she was seen by me. Her blood pressure was 190 systolic and 110 diastolic. She relaxed under the action of the apparatus in a marked way and slept soundly each time. Before treatment the blood pressure was 190 systolic and 110 diastolic, 165 systolic and 105 diastolic, 140 systolic and 90 diastolic, 170 systolic and 90 diastolic, 150 systolic and 80 diastolic, etc.; after treatment: 140 systolic and 90 diastolic, 120 systolic and 80 diastolic, 120 systolic and 80 diastolic, 130 systolic and 80 diastolic, 140 systolic and 70 diastolic, etc.

After a number of treatments, her headaches and other subjective symptoms disappeared.

There is little doubt of the existence of permanent pathologic changes in the blood vessels of the patient in case 5. Muscular relaxation, however, was strikingly adequate in reducing the resistance offered to the arterial flow. A possible explanation is that in addition to a permanent thickening of the wall of the arterioles, a further narrowing of their lumen took place as a result of supernormal nerve impulses acting on their musculature. Another possible explanation may be sought in the tension of the voluntary musculature causing a constriction of the capillary bed in that situation. Plausible, however, as this appears from a mechanical point of view, it is not borne out by

clinical evidence offered by certain muscular rigidities of the parkinsonian state, of residual hemiplegia and of other conditions in which the blood pressure may be normal.

The action of inhibition of nerve impulses caused by the rhythmic wave of pressure exerted by the apparatus may be invoked to explain the reason why it is more effective in reducing the blood pressure in proportion as it is higher in those instances in which it is at all effective. In cases in which the high blood pressure is due to abnormally strong neural impulses acting on the musculature of the arterioles, an inhibition of those impulses must result in a lowering of the pressure. Higher pressures would therefore be reduced to a greater degree than would lower pressures.

In all cases of hypertension with cardiac hypertrophy from any cause, the sharp, ringing heart sounds are changed during the treatment described so that they approach normal.

Respiratory System.—During the treatment, the respiratory movements are those of the resting person. No studies have been made of the effect of the treatment for diseases of this system.

In hooking up the body part of the garment about the person, it was found that most people find it disagreeable when it is at all tight about the upper part of the chest. It was thought at first that the reason for this is that as the garment tightens in successive rings it impedes the inspiratory movements. On further study, however, it was found that such was not the case. The mere touch of the peristaltic wave of the garment on the upper part of the chest is disagreeable to some persons. It appears that the differences in the time between the rhythmic movements of the garment and those of the respiratory movements is the source of the disagreeable sensation.

SUMMARY AND CONCLUSIONS

An apparatus is described the action of which consists in a wave of encircling pressure applied to the periphery of the body and the limbs in the direction of the venous flow. The most striking and uniform effect is muscular relaxation and, in most persons, sleep. These effects are ascribable to a physiologic state of nerve inhibition. But the manner in which the wave of circular compression exercised on the periphery affects the nervous system so as to cause a general state of nerve inhibition is not yet understood.

Subjected to the action of the apparatus a number of times, persons appear to contract the habit of relaxation. They rest better at night and they go about their business or pleasure, as the case might be, in a more deliberate and systematic manner. Whether as a result of this, or perhaps in consequence of the direct action of the apparatus in

driving onward the contents of the peripheral veins and lymphatics, the general nutrition is enhanced.

During the action of the apparatus the blood pressure, both systolic and diastolic, is reduced in certain cases, but remains unaltered in others. In still other cases, reduction takes place at certain times and does not at other times. Since the most obvious action of the apparatus is the induction of a general state of nerve inhibition, it is reasonable to conclude that instances of hypertension reducible by means of the apparatus are due to supernormal neural impulses acting on the musculature of the arterioles. By the same token the conclusion is reasonable that hypertension not affected by the action of the apparatus is due to a permanent change in the tissue of the arterioles, and instances reducible at certain times and not reducible at others are due neither to strong neural impulses nor to a permanent pathologic change, but to certain substances the occasional presence of which in the blood acts directly on the musculature of the arterioles.

NERVOUS AND MENTAL PHENOMENA ACCOMPANYING INSULIN THERAPY*

ELMER L. SEVRINGHAUS, M.D.
MADISON, WIS.

One of the most pleasing results of insulin therapy in some of the diabetic patients is the change from a morose to a cheerful frame of mind. This new cheerfulness may be induced by the good prognosis which is given to the patient who cooperates in a program of dietetic and insulin control. Aside from this, however, there is evident a marked, prompt change in some patients with the more severe cases of diabetes when treatment with insulin stops the loss of sugar and causes the metabolic processes to run once more in normal channels. This change led Cowie, Parsons and Raphael[1] to a study of the sugar tolerance in the two phases of manic-depressive psychoses. They reported that the sugar tolerance is reduced in the depressive phase, and that it is changed toward the normal by the administration of insulin. Whether this will be of use in the therapy of the psychosis remains to be seen.

On the other hand, the use of too much insulin in some diabetic persons has caused a change from the normal disposition to one of irritability and restlessness resembling that of a hungry child. Although to the members of the family this may seem a permanent change, it is only temporary. A return to the normal disposition occurs as soon as the dosage of insulin and the diet are properly adjusted to avoid a continuous mild hypoglycemia.

The symptoms of an excessive dosage of insulin are, with few exceptions, referable to a disturbed activity of the central nervous system. The probable exceptions are hunger and muscular weakness. Hunger appears to be a sensory result of gastric contractions brought on by reduction in the amount of sugar available for the gastric muscles. Muscle weakness may be related to the same causative factor. It is conceivable, however, that either or both these symptoms may be due, in part, to a direct effect on the central nervous system. At any rate, the other manifestations of hypoglycemia are the expressions of stimulation or disturbance of functions of the central nervous system. It is

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* Read at a Meeting of the Central Neuropsychiatric Association, Madison, Wis., Oct. 27, 1928.

* From the Department of Medicine, and the Wisconsin General Hospital, University of Wisconsin.

1. Cowie, D. M.; Parsons, J. P., and Raphael, T.: Insulin and the Mental State of Depression, Arch. Neurol. & Psychiat. **12**:522 (Nov.) 1924.

commonly suggested that these phenomena are concerned with the sympathetic and autonomic systems. A grouping of the symptoms will show that the effects are far more widely diffused in the nervous system.

The following evidences of hypoglycemia probably indicate stimulation in the vegetative nervous system: flushing or pallor, sweating, pupillary changes, tachycardia and increased blood pressure. These are among the commoner and the earlier symptoms. It has been shown that stimulation via the splanchnic nerves is the means by which the suprarenal glands are caused to deliver more of their secretion to the circulation.[2] The effects on these glands have been studied not alone by physiologic experiments, but also morphologically.[3] Convulsions are not a necessary condition of the suprarenal response.[3] The suprarenal activity is the mechanism by which tachycardia, increase in blood pressure and liberation of glycogen from the liver are brought about. This is a fortunate teleologic mechanism. It is undoubtedly in use several times daily as a consequence of the hypoglycemia that follows the hyperglycemia caused by the ingestion of carbohydrate foods by normal persons. The unusual case of a patient under insulin therapy who was treated for hyperthyroidism, reported by John,[4] probably involves the activity of the suprarenal glands under frequent, if not continuous, overdosage of insulin.

In the field of sensory phenomena one notes numbness, coldness and paresthesias of the extremities. Special senses are involved in amblyopia, tinnitus and vertigo. The early motor involvements are tremulousness, muscle incoordination and fine tremors, phenomena that involve also muscle-position sense. In more pronounced cases, there may be twitching, convulsions of tonic and clonic types and hemiplegias, partial or complete. The hemiplegic reactions have recently been described by several authors.[5] These hemiplegias, like the other phenomena following treatment with insulin, are transient. Recovery either has been spontaneous or has been induced by the administration of dextrose.

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2. Cannon, W. B.; McIver, M. A., and Bliss, S. W.: Studies on the Conditions of Activity in Endocrine Glands: XIII. A Sympathetic and Adrenal Mechanism for Mobilizing Sugar in Hypoglycemia, Am. J. Physiol. **69**:46, 1924.

3. Kahn, R. H.: Ueber die zentrale Reizung der Nebennieren und der Paraganglien während der Insulinvergiftung, Virchows Arch. f. d. ges. Physiol. **212**: 54, 1926.

4. John, H. J.: Hyperinsulinism, Surg. Gynec. Obst. **44**:190, 1927.

5. Ashe, B. I.; Mosenthal, H. O., and Ginsberg, G.: Hypoglycemia with and without Insulin, with and without Symptoms, J. Lab. & Clin. Med. **13**:109, 1927. Miller, W. L., and Trescher, J. H.: Amnesia, Epileptiform Convulsive Seizures, and Hemiparesis as Manifestations of Insulin Shock, Am. J. M. Sc. **174**:453, 1927. Ravid, J. M.: Transient Insulin Hypoglycemic Hemiplegias, ibid. **175**:756, 1928.

The convulsions have been variable in type and in distribution among muscle groups. A similarity to the convulsions of tetany has been suggested by several authors.[6] Five years ago, McPhedran and Banting [7] mentioned a reduction in the tendency to severe reactions following the use of calcium lactate in both animals and children. This therapy is evidently not common practice now. These authors stated that calcium therapy did not elevate the concentration of sugar in the blood even though it was effective. In the Wisconsin General Hospital, Dr. O. O. Meyer recently saw a rather marked reaction to insulin, which surprisingly resembled tetany. The paresthesia, spontaneous twitching in the facial and forearm groups, pain in these regions, carpal flexor spasm and positive Chvostek sign were all observed. The blood taken during the display of symptoms contained 11.7 mg. of calcium per hundred cubic centimeters of serum, which is a high normal level. Relief from the symptoms was obtained by the use of considerable amounts of dextrose. The following day, a less marked picture of the same type appeared and was quickly aborted by orange juice. It is apparent that the reaction to insulin did not operate by producing a low concentration of calcium, although it may conceivably have caused a temporary low concentration of the calcium ions, a question which cannot yet be determined experimentally. A simpler explanation of these relationships is that hypoglycemia acts as an irritant to motor nerves, and that the response is tetany-like. Increased concentration of calcium ions reduces this irritability, as is well known. Administration of calcium raises this concentration and reduces the response to irritation. The reduction can be accomplished also by any anesthetic, by depressant drugs or by other means that reduce irritability of the nerves. This means merely that a specific antagonism does not exist between insulin and calcium or between the islands of Langerhans and the parathyroid gland, and that the suppression of hypoglycemic responses is pharmacodynamic rather than physiologic. Similar reasoning applies to the antagonism between insulin and pituitary or any other of the so-called "gluco-augmentors" of Levai and Waldbauer.[8]

There are numerous psychic phenomena resulting from insulin given in excess relative to the dextrose available. Restlessness and the late coma were recognized almost at the start. More recently there have

6. Miller and Trescher (footnote 5, second reference). Winogradow, W. W., and Steinberg, S. J.: Ein Fall von Hypoglykämie mit tödlichem Ausgang, Klin. Wchnschr. **6**:1338 (part 2) 1927.

7. McPhedran, A., and Banting, F. G.: Insulin in Treatment of Severe Diabetes, J. A. M. A. **80**:1726 (June 9) 1923.

8. Levai, M., and Waldbauer, O.: Die Beeinflüssbarkeit des Blutzuckers beim Kaninchen, Deutsche med. Wchnschr. **52**:101, 1926.

been reports of a loss of inhibitions, emotional disturbances,[9] hallucinations, amnesia,[10] aphasia, peculiar confusional states, catatonia and negativism. These occurrences have led to humorous as well as embarrassing and unfortunate accidents. The similarity of the reaction to alcoholic intoxication has led to mistakes even within a hospital.[11] The ease with which such a difficulty may occur is shown by the history of an intelligent young man who had been using insulin for five years. One evening he planned to take a 6 o'clock train from Chicago to Milwaukee, a two hour ride. He injected the usual dose of insulin and planned to get his supper at the depot restaurant, but was delayed. He had time only to get on his train without even a bit of fruit. Although aware of the onset of a reaction to insulin he said nothing. Arriving in Milwaukee, he was just able to direct the driver of a taxicab to take him to a hospital where he was known. When the driver arrived, the patient was acting like an inebriate and was therefore taken to the emergency ward for treatment for alcoholism. The stomach pump had been tried before some one recognized the patient, guessed the riddle and administered the dextrose that brought relief. Sjögren and Tillgren [9] related how one patient was "making somersaults in his bed," resisted help and gave the appearance of having hysteria until the attack spontaneously subsided. The catatonic state induced by hypoglycemia was described in an earlier report.[12]

These manifold evidences of insulin in relative excess are cited to show the widespread effect of hyperinsulinism. There is nothing specific about the picture except the circumstances under which it is induced; nevertheless, in a given patient, it tends to run more or less true to type. Diagnostically, the variability of the picture makes a great deal of confusion. Once a patient has learned to know how a relative excess of insulin affects him, he is fairly well prepared to meet the emergency later. This is not absolutely true, since only the milder aspects of the vegetative functions may be involved in the trial reactions that are often induced in hospitals as a matter of training the patient. Later, the psychic manifestations may occur in an insidious manner, without the patient's understanding the cause. It is wise to inform a diabetic patient who is taking insulin that any occurrence out of the ordinary should be considered a possible reaction to insulin.

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9. Sjögren, T., and Tillgren, J.: On Peculiar States of Confusion in Insulinism, Acta med. Scandinav. **65**:684, 1927.

10. Sevringhaus, E. L.: Hypoglycemic Coma Due to Repeated Insulin Overdosage, Am. J. M. Sc. **172**:573, 1926; Difficulties in the Diagnosis of Insulin Coma, J. A. M. A. **91**:305 (Aug. 4) 1928. Harrop, G. A.: Hypoglycemia and the Toxic Effects of Insulin, Arch. Int. Med. **40**:216 (Aug.) 1927.

11. Sevringhaus (footnote 10, second reference).

12. Sevringhaus (footnote 10, first reference).

Even if the urine cannot be tested at once, a therapeutic trial of sugar for relief may be resorted to with safety. This must, of course, be used with discretion by those patients who look for excuses that will allow a dietary excess.

It is interesting to speculate as to the cause of these reactions to insulin. Ravid [13] suggested a direct effect of insulin on the nerve cells, intoxication by intermediate carbohydrate metabolites or the "sugar vacuum" most commonly supposed. The first cannot be the cause since these phenomena all occur in cases in which there is no change in the amount or the type of insulin administered, but in which the intake of carbohydrates is notably reduced. The second is for the same reason improbable, since, under these circumstances, the amount of intermediate metabolites would probably be reduced. In this case, however, the reasoning is not conclusive. The sugar vacuum is a reasonable explanation which is made more reasonable by the demonstration that the brain contains little dextrose but oxidizes much of the dextrose, obviously supplied by the blood. The dependence of the brain on blood dextrose is analogous to its dependence on blood oxygen. In fact, many of the symptoms of hypoglycemia can be produced likewise by anoxemia. The rate of reduction in the supply of oxygen controls the type of response, whether excitement or depression. The same seems true in the case of insulin. The symptoms are known to occur at various blood sugar levels, and to be induced at higher levels by rapidly falling blood sugar concentrations.[14]

It will be of some interest to know that death following excessive doses of insulin is accompanied by visible changes in the brain. Of the few cases that have been reported, two were reported by Wohlwill,[15] who performed necropsies on the brains. In one case there was shown a paresis of the seventh nerve due to insulin. Focal disease was not found. The brains were grossly dry and friable. Microscopically, they showed evidence of severe cellular damage, with swelling, which was probably the cause of the gross dryness and friability. The nuclei and the cytoplasm showed striking evidences of degeneration. This was thought to be more than the change that takes place in the equivalent time post mortem in ordinary cases. The ameboidosis of the glia cells was greatly exaggerated. In the patient with the paresis of the seventh nerve there were changes in the axis cylinders, but the changes were symmetrical and included nerves other than the seventh and its roots. All these changes in the nerve cells have been produced by diabetic

13. Ravid (footnote 5, third reference).

14. John, H. J.: Insulin Reactions, J. M. Research **7-8**:51, 1926.

15. Wohlwill, F.: Ueber Hirnbefunde bei Insulin-überdosierung, Klin. Wchnschr. **7**:344, 1928.

acidosis, by alkalosis and by other chemical injury. The pathologic changes are not specific, but indicate a physical basis for the functional changes in life. Such changes are probably reversible unless the hypoglycemia has been of too long a duration. This is in the same sense that the changes due to anoxemia may or may not be reversible.

The neurologist may be able to point out correlations that have not already been mentioned. It appears, however, that the nerve structures which are affected in a given case of excess of insulin are not any narrowly specific ones, nor are they limited to certain parts of the nervous system to the exclusion of other parts. The suggestion is made that, in any case, the response will be from those parts of the body that are most easily stimulated or depressed. This hypothesis involves at least two corrolaries: (1) that the symptoms will follow in a sequence, (2) that the sequences will vary in different persons. The sequence in a given person will tend to be of a definite type, because the susceptibility to stimulation is, in part, a characteristic. This typical sequence is generally observed. The variability of sequences in persons is not more surprising than the variability in response to any other stimulus capable of as wide an effect as hypoglycemia can have. The only conditions to be compared with it are carbon monoxide poisoning or any other type of anoxemia, alcoholic intoxication, thyrotoxicosis, cerebral vascular accidents, epilepsy, uremia and dementia, particularly of the catatonic type. These are the conditions with which reactions to insulin are apt to be confused. In diagnosis of coma without a history, the possibility of a coma due to hypoglycemia must be considered. If an analysis of the blood cannot be secured at once, it should be remembered that the therapeutic trial of dextrose given intravenously is never dangerous and may be saving. At least 20 cc. of a 50 per cent solution of sterile pure dextrose should be given. The result will be recovery within a few minutes, if hypoglycemia is the cause. Many times the physician's hesitation in administering dextrose to a diabetic patient is caused by his fear that an overdose of dextrose may transform coma due to insulin into a diabetic acidosis and coma. There is no basis in fact for any such fear. A single dose of sugar will never cause a diabetic person to develop coma. It should be used without hesitation when hypoglycemic reactions occur.

MALARIA AS A THERAPEUTIC AGENT FOR PARESIS

AN ANALYSIS OF ONE HUNDRED AND ONE PATIENTS TREATED AT THE WORCESTER STATE HOSPITAL *

CESAREO DEASIS, M.D.
WORCESTER, MASS.

The treatment for paresis with malaria was first given a trial in 1917 by von Jauregg, of Vienna, and the favorable results obtained justified its further use, at least as a clinical experiment. The past eleven years have found many clinicians and laboratory workers making investigations in the same field. Encouraging results have been obtained, but this mode of therapy has not as yet been placed on a firm basis, and its ultimate result has not been fully established.

It is a common occurrence in a mental ward for a psychotic patient to show some mental lucidity during or soon after a febrile condition resulting from a common disease such as influenza or pneumonia. This clinical fact has been known for ages, and even the layman has come to recognize it. Hippocrates referred to the value of fever in alleviating psychotic symptoms. In the Middle Ages, when insanity was considered the work of the devil, cognizance was taken of the efficacy of fever in the relief, temporarily at least, of psychotic conditions, and the formation of boils and abscesses by inoculation or otherwise was encouraged among the insane to produce fever for that purpose. Louis XI, who had epilepsy, craved the administration of quartan malaria. In the modern period, Robert Louis Stevenson referred to fever as a stimulant to dull nerves into something of their old quickness and sensibility.

My object in this paper is to report the individual cases of paresis in which the patients were treated at the Worcester State Hospital since Aug. 1, 1925 (table 1).

TECHNIC OF ADMINISTRATION

The type of malaria used is the benign tertian. The method of inoculation is simple. Typing of the bloods of the donors and recipients is not necessary. Strict asepsis is observed throughout. The cubital fossa, the usual site for venipuncture, is sterilized with alcohol. To prevent coagulation, sodium citrate solution (from 1 to 1.5 cc.) is drawn into the syringe with the blood. This citrated blood is given intravenously to the recipient with the least possible delay. It is my practice, when possible, to have the donor and the recipient in the same ward during the operation.

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Time of Collection of Blood for Inoculation.—To some clinicians it seems immaterial whether the blood is drawn before, during or after a chill. I have tried each of the three different periods and have found that blood collected during the chill or while the temperature is above 104 F. gives the best results; the incubation period is materially shortened and the first paroxysm (not the initial rise of temperature due to the presence of foreign protein) may be expected at any time after twenty-four hours. The appearance of the first chill twenty-four hours after inoculation, and followed by chills every other day, is fairly common in my experience.

Care of the Patient with Malaria.—As a rule, general care is all that is necessary. Complications which will be discussed later are carefully watched for and treated expectantly.

How Many Chills Should a Patient Have?—The question as to how many chills a patient should have is commonly asked. Some allow a patient to have as many as twenty-two. Eighteen is the most allowed at this hospital. If the "baking" effect of the fever, which some believe to be the essential factor in the destruction of the spirochetes, is what determines the clinical results, it would seem logical to think that the more paroxysms there are the better the results will be. This is not borne out, however, by clinical experience. Some of my best clinical results were obtained from a few chills, others from a higher number; patients showing improvement had had as many or as few chills as patients showing aggravation. There is, therefore, no apparent relationship between the clinical results and the number of paroxysms. The only criterion used at this hospital in deciding how many chills a patient should have is his general condition. We allow from eight to eighteen chills in any given case.

Treatment for Malaria.—If the patient has had enough chills or if his condition is such that further paroxysms would endanger his life from intercurrent infection or organic conditions, 10 grains (0.65 Gm.) of quinine sulphate is administered by mouth three times a day for a week, and 5 grains (0.32 Gm.) three times a day for the following week. This is followed routinely by elixir of iron, quinine and strychnine, N. F., 1 dram, three times a day, for a month. I have had no difficulty in checking the paroxysms. I do not recommend the intravenous administration of quinine on account of the reactions that follow the injection, reactions that are due presumably to the liberation of foreign protein on the destruction of parasites.

INCIDENTS AND COMPLICATIONS DURING THE COURSE OF TREATMENT

Herpes Labialis.—This eruption is common and was present in the great majority of the patients included in this series.

TABLE 1.—*Analysis of 91 Patients*

Marginal Number	Case Number	Age and Sex	Date of Admission	Probable Date of Infection	Probable Date of First Symptoms	Date of First Chill	Date of Last Chill	Number of Chills	Serology *							
									Spinal Fluid Cell Count		Globulin Test		Wassermann Test		Colloidal Gold	
													Blood	Spinal Fluid		
									Before Treatment	After Treatment	Before Treatment	After Treatment	After Treatment	After Treatment	Before Treatment	After Treatment
1	36935	40-M	2/ 9/26	.....	12 yr.	5/11/26	6/11/26	13	High	Normal	..	—	+	+	..	Al
2	37052	50-M	4/22/26	.....	18 mo.	6/ 6/26	6/22/26	15	High	Normal	+	+	..	..	I	..
3	35193	47-M	7/ 6/23	.....	2 wk.	6/14/26	7/19/26	8	High	High	+	+	+	+	Al	Al
4	36804	43-M	11/16/25	.....	.....	12/29/25	1/ 9/26	9	High	.....	+	..	..	..	..	..
5	33158	47-M	4/28/20	.....	.....	7/ 4/23	8/ 8/26	14	Normal	.....	+	+	+	+	I	I
6	36204	49-M	3/11/25	.....	.....	5/30/26	6/19/26	17	Normal	Normal	+	+	+	+	Al	I
7	36370	47-M	4/23/25	.....	.....	5/29/26	6/ 6/26	18	Normal	Normal	+	+	+	+	I	I
8	36186	43-M	7/24/23	.....	.....	5/ 2/26	6/19/26	18	High	Normal	+	+	+	+	I	I
9	37098	35-F	5/28/26	.....	1 mo.	8/ 8/26	8/30/26	16	Borderline	.....	+	..	+	..	I	..
10	37046	54-F	4/20/26	.....	18 mo.	7/ 6/26	7/27/26	15	High	Normal	+	—	+	—	I	Flat
11	36299	35-M	3/27/25	10 yr.	1 yr.	8/19/25	9/ 8/25	11	Normal	Normal	+	+	+	—	I	I
12	36977	51-M	3/ 4/26	.....	6 yr.	5/ 6/26	7/23/26	15	High	Normal	+	+	..	+	I	I
13	35828	38-M	2/ 8/24	.....	12 yr.	9/25/25	10/10/25	10	Normal	Normal	+	+	—	+	I	I
14	36555	37-M	7/14/25	.....	.....	1/12/26	1/22/26	11	Normal	Normal	+	+	+	+	I	I
15	36536	74-M	7/ 6/25	.....	.....	6/ 2/26	7/15/26	6	Normal	Normal	+	+	+	+	I	I
16	35493	46-M	11/18/23	.....	.....	7/19/26	7/24/26	3	Borderline	.....	+	..	..	..	I	..
17	36136	37-M	1/12/25	8 yr.	8 yr.	11/21/25	12/ 6/25	11	Normal	Normal	+	+	+	+	I	I
18	36216	30-M	3/17/25	.....	.....	9/29/25	10/23/25	7	Normal	.....	+	..	..	..	I	..
19	36185	48-M	2/22/25	.....	5 yr.	6/22/26	7/11/26	18	Normal	Normal	+	+	+	+	I	I
20	36521	32-M	6/22/25	.....	.....	(Dates not available)		12(?)	Normal	Normal	+	+	..	..	I	I
21	30686	38-M	8/ 4/25	.....	4 yr.	10/17/25	11/ 2/25	13	High	Normal	+	+	+	+	I	I
22	36243	30-F	3/19/25	.....	.....	5/31/26	6/12/26	9	Normal	Normal	+	—	—	+	I	I
23	35983	40-M	9/14/24	.....	.....	5/ 7/26	6/ 4/26	17	Normal	Normal	+	+	—	+	I	I
24	37184	50-M	4/25/17	.....	3 yr.	8/18/26	9/13/26	6	Normal	Normal	—	—	+	+	I	I
25	36655	56-M	8/12/25	.....	.....	11/12/25	12/ 4/25	15	Normal	Normal	+	+	+	+	I	I
26	36190	41-M	3/ 2/25	16 yr.	2 yr.	5/ 9/26	5/25/26	17	Normal	Normal	+	+	+	+	I	I
27	36695	35-F	9/ 9/25	15 yr.	4 yr.	11/29/25	12/26/25	14	Normal	Normal	+	+	+	—	I	I
28	36440	52-M	5/19/25	.....	.....	5/24/26	6/13/26	9	Normal	.....	+	..	+	+	I	..
29	36431	35-M	5/ 7/25	.....	5 wk.	8/ 4/26	9/ 4/26	11	High	.....	+	..	+	+	I	..
30	35043	29-M	8/25/24	11 yr.	1 mo.	10/16/25	11/ 6/25	13	Normal	.....	+	..	..	+	I	I
31	36958	36-M	2/22/26	.....	13 mo.	5/ 7/26	5/11/26	3	.....	.....	+	+	—	+	I	Al
32	37128	50-M	6/ 8/25	.....	8 yr.	7/14/26	8/ 6/26	14	Borderline	.....	+	—	—	+	I	I
33	36177	28-M	2/ 9/25	.....	7 mo.	1/18/25	1/21/25	4	Normal	Normal	+	+	+	+	I	I
34	35972	41-M	9/15/24	.....	.....	5/19/26	6/ 4/26	15	Normal	.....	+	..	+	..	I	I
35	36099	49-M	12/13/24	.....	.....	5/20/26	6/25/26	18	High	Normal	+	+	+	+	I	I
36	35428	43-M	10/16/23	.....	5 mo.	5/10/26	5/27/26	11	High	.....	+	+	+	+	I	I
37	36766	35-M	10/22/25	.....	.....	12/13/25	12/22/25	10	High	Normal	+	—	—	+	I	I

* In this table, under the heading of spinal fluid cell count, normal indicates from 1 to 8 cells, borderline indicates from 9 to 15 cells, and high indicates more than 15 cells. Under the heading colloidal gold, I indicates a paretic curve, Al an atypical paretic curve, and Flat a normal curve.

Neurologic Observations on Admission	Mental Status on Admission	Mental Status after Malarial Therapy	Present Status
Pupils unequal; right pupil rigid.....	Apathetic, uncommunicative, irrelevant; has auditory hallucinations and persecutory delusions	Very much improved; no false perceptions	Visit 2/22/28
Gait unsteady	Nervous, apprehensive, suspicious; defective memory	Very much improved	Visit 11/8/27
Pupils sluggish; knee reflexes hyperactive	Masked face; no insight; depressed; no false perceptions	Improved.....	Hospital
Pupils unequal; knee reflexes hyperactive; gait unsteady	No insight	.....	Died 1/11/26
Knee reflexes hyperactive; tremors of lips and fingers; speech defective	Confabulations; disorientation; poor memory	Not improved.....	Hospital
Rombergism; knee reflexes hyperactive	Disoriented; filthy; no insight; auditory hallucinations	Not improved.....	Hospital
Pupils unequal, irregular, rigid; knee reflexes unequal; speech defective	Retarded; apathetic; unresponsive; deteriorated	Not improved.....	Hospital
Pupils irregular; knee reflexes hyperactive; speech defective	Confabulations; no insight; bizarre ideas	Very much improved; insight regained	Visit 9/19/27
Pupils unequal, irregular; speech defective	Destructive, untidy, confused and restless	Improved.....	Hospital
Pupils unequal; knee reflexes hyperactive	Disoriented; memory defective; no insight; confabulations	Improved.....	Hospital
Pupils sluggish; knee reflexes hyperactive	Assaultive; bizarre ideas.....	Very much improved	Visit 1/27/26; discharged 1/27/27; committed suicide
Pupils sluggish; speech slow; knee reflexes unequal	Paranoid ideas; chiefly persecutory.....	Improved slightly....	Deported to Canada 9/27/26
Knee reflexes absent; Rombergism; gait unsteady; pupils irregular	Euphoric; no insight; confabulations; grandeur	Very much improved	Visit 12/13/25; discharged 12/13/27
Marked speech defect.....	Talkative; confused	Not improved.....	Died 5/18/28
No marked signs.....	Talkative, assaultive, confused and disoriented	Not improved.....	Hospital
Pupils unequal, irregular, rigid; knee reflexes hyperactive	Confused; no insight; bizarre ideas.....	.....	Died 7/24/26
Pupils sluggish; knee reflexes hyperactive	Disoriented; restless; childish; euphoric; no insight	Not improved.....	Hospital
Pupils unequal, rigid; Rombergism	Grandeur; masked face.....	.....	Died 11/4/25
No marked signs.....	Confabulations	Not improved.....	Hospital
Knee reflexes hyperactive on one side; tremors of lips, hands and tongue; speech defective	Euphoric; disoriented	Very much improved	Visit 11/8/25; discharged 11/8/26
General hyperreflexia; tremors of fingers; speech defect	Assaultive; overactive	Very much improved	Visit 3/19/26; discharged 3/19/27
Pupils unequal, irregular, sluggish; knee reflexes hyperactive; speech defect	Auditory hallucinations; grandiose and persecutory ideas	Not improved.....	Hospital
Pupils unequal, irregular, sluggish; knee reflexes absent	Judgment impaired	Not improved.....	Died 3/26/28
Pupils unequal, sluggish; knee reflexes absent	Disoriented for time; bizarre ideas.....	Not improved.....	Hospital
Pupils unequal, irregular, sluggish; knee reflexes absent; Rombergism	Euphoric; silly; untidy; unstable emotionally; no insight	.....	Died 10/25/26
Knee reflexes unequal.....	Euphoria; flighty ideas; grandeur.....	Not improved.....	Hospital
Pupils unequal, irregular, sluggish; knee reflexes hyperactive	False perceptions; grandeur; disorientation; poor judgment	Not improved.....	Hospital
Pupils rigid; knee reflexes hyperactive	Silly; disoriented; no insight.....	Not improved.....	Died 7/12/26
Pupils irregular; knee reflexes hyperactive	Disoriented; overactive	.....	Died 9/9/27
Pupils unequal; knee reflexes hyperactive	Euphoric; overactive; destructive; homicidal	Very much improved	Visit 1/10/27; discharged 1/10/28
No marked signs.....	Silly; overactive; destructive; no insight	Very much improved	Visit 8/25/26; discharged 8/25/27
Pupils sluggish; knee reflexes hyperactive; gait unsteady	Confabulations; grandeur; overactivity; bizarre ideas	Very much improved	Visit 3/18/28
No marked signs.....	Auditory hallucinations	Very much improved	Escaped 6/4/27
Pupils unequal, irregular, sluggish; knee reflexes absent	Euphoric; destructive; assaultive; grandiose ideas	.....	Died 7/28/26
Left pupil irregular and rigid; knee reflexes absent	Demented and totally disoriented.....	Not improved.....	Hospital
Pupils unequal and sluggish to light; knee reflexes unequal	Emotionally dull; auditory hallucinations	Not improved.....	Hospital
Knee reflexes hyperactive; speech defective; tremors of fingers	Euphoric; egoistic; restless; grandiose ideas	Improved slightly....	Died 6/26/27

TABLE 1.—*Analysis of 10*

Marginal Number	Case Number	Age and Sex	Date of Admission	Probable Date of Infection	Probable Date of First Symptoms	Date of First Chill	Date of Last Chill	Number of Chills	Serology *							
									Spinal Fluid Cell Count		Globulin Test		Wassermann Test		Colloidal Gold	
													Blood	Spinal Fluid		
									Before Treatment	After Treatment	Before Treatment	After Treatment	After Treatment	After Treatment	Before Treatment	After Treatment
38	30478	40-M	6/ 5/25	.....	.....	4/29/26	5/25/26	16	Normal	Normal	+	+	+	—	I	I
39	35773	37-F	5/23/24	.....	.....	10/ 2/26	10/14/26	13	Normal	.....	+	..	..	+	I	I
40	35563	28-M	12/22/23	.....	11 mo.	9/23/25	11/ 7/25	11	Normal	.....	+	..	..	+	I	..
41	36118	42-M	12/29/24	.....	.....	6/23/26	6/27/26	5	Normal	.....	+	..	+	+	I	I
42	36851	45-F	12/17/25	.....	2 mo.	6/ 2/26	6/ 9/26	8	Borderline	Normal	+	—	—	—	I	I
43	34742	44-M	11/27/22	.....	6 mo.	8/ 1/26	8/13/26	13	Normal	Normal	+	+	+	+	I	..
44	36462	27-M	6/ 3/25	.....	3 wk.	8/29/25	9/11/25	8	High	Normal	+	+	..	+	I	I
45	33805	25-M	11/22/22	.....	6 mo.	12/25/25	1/ 8/26	14	Normal	.....	+	..	..	..	I	..
46	36398	36-F	4/23/25	.....	4/5/25	8/ 4/25	8/30/25	8	High	Normal	+	..	..	..	I	I
47	36507	53-M	6/ 6/25	.....	.....	6/25/26	7/14/26	10	Borderline	Normal	+	+	+	+	I	I
48	36707	36-M	9/11/25	8 yr.	6 mo.	10/30/25	11/ 4/25	14	High	High	+	+	+	+	I	I
49	37473	47-M	2/12/27	.....	3 yr.	2/25/27	3/21/27	19	Normal	.....	—	..	..	..	I	..
50	37458	43-M	2/11/27	.....	6 mo.	3/ 1/27	3/16/27	11	Borderline	.....	+	..	+	..	I	..
51	37837	35-M	9/13/27	.....	16 mo.	10/28/27	11/ 9/27	4	Normal	Normal	+	+	+	+	I	I
52	37601	41-M	4/29/27	.....	9 mo.	5/26/27	7/ 8/27	6	Normal	.....	—	..	..	..	I	..
53	37571	52-M	4/10/27	.....	4 mo.	5/17/27	5/20/27	3	Normal	.....	—	..	..	..	I	..
54	37412	42-M	1/17/27	.....	5 mo.	11/26/26	12/15/26	11	Borderline	Normal	+	+	+	+	I	I
55	37017	48-F	4/ 3/27	.....	6 mo.	12/10/26	12/17/26	8	High	.....	+	+	+	+	I	I
56	37346	40-F	11/30/26	.....	2 wk.	12/28/26	1/14/27	13	Normal	.....	+	..	..	..	I	..
57	37191	37-M	8/ 5/27	.....	2 yr.	9/18/26	10/ 5/27	16	High	.....	+	+	.	+	I	I
58	37742	42-M	7/25/27	.....	.....	8/ 6/27	11/23/27	11	.....	.....	+	..	+	..	..	..
59	37817	38-M	9/ 8/27	8 yr.	8 yr.	10/19/27	11/21/27	15	.....	.....	+	..	..	..	I	..
60	37506	48-M	3/ 5/27	10 yr.	10 yr.	4/ 8/27	4/25/27	16	Normal	.....	+	+	—	+	I	I
61	37791	44-M	10/27/27	.....	4 yr.	10/24/27	11/26/27	15	.....	Normal	+	+	—	+	I	I
62	37675	31-M	6/16/27	8 yr.	8 yr.	9/14/27	10/22/27	12	Normal	Normal	—	+	+	+	I	I
63	37397	43-F	1/ 6/27	.....	3 mo.	3/20/27	3/30/27	8	Normal	.....	+	..	+	+	I	..
64	37318	35-M	4/ 8/26	9 yr.	1 yr.	4/26/26	5/21/26	16	High	Normal	+	+	—	+	I	I
65	37702	30-F	8/ 8/27	.....	8 mo.	8/19/27	9/ 4/27	11	.....	Normal	+	+	+	+	I	Flat
66	37399	32-M	12/25/26	.....	14 yr.	2/ 8/27	2/16/27	9	High	.....	+	..	+	..	I	..
67	37805	34-M	9/ 6/27	9 yr.	5 mo.	11/14/27	12/ 3/27	16	.....	Normal	+	+	—	+	I	I
68	37272	29-F	9/22/26	10 yr.	10 yr.	11/ 3/26	11/20/26	11	.....	.....	—	..	+	..	I	..
69	37560	33-F	4/ 1/27	10 yr.	10 yr.	Had several slight chills simulating but not typical of malaria			Normal	.....	+	..	..	..	I	..
70	37518	48-M	3/10/27	.....	.....	4/15/27	5/19/27	11	.....	Normal	..	+	+	—	..	I
71	37726	30-M	7/ 6/27	.....	4 mo.	No chills after repeated inoculation			.....	Normal	..	+	+	+	I	I

Patients Treated—Continued

Neurologic Observations on Admission	Mental Status on Admission	Mental Status after Malarial Therapy	Present Status
Pupils unequal, irregular and rigid	Apathetic; disoriented; no insight	Improved slightly; relapsed	Visit 5/3/27; returned 6/1/28
Pupils sluggish; knee reflexes hyperactive; clonus	Disoriented; no insight	Very much improved	Visit 3/17/26; discharged 3/17/27
Pupils sluggish; knee reflexes hyperactive	Grandiose ideas; poorly oriented	Very much improved	Visit 10/26/26; discharged 10/26/27
Speech defective; tremors; knee reflexes hyperactive	Euphoric; disoriented	Not improved	Hospital
No marked signs	Manic train of thought; emotional instability	Very much improved	Visit 12/23/25; discharged 12/23/26
Pupils unequal, irregular, rigid; knee reflexes hyperactive	Euphoric; poor judgment	Not improved	Died 6/16/27
Pupils rigid	Fabrications; grandeur; auditory hallucinations; euphoria	Very much improved	Visit 1/25/25; discharged 1/25/26
Knee reflexes hyperactive; tremors of tongue; speech defect; incoordination	Confused; no insight		Died 2/15/23
Pupils unequal	Grandiose and bizarre ideas; auditory hallucinations	Very much improved	Visit 10/22/25; discharged 10/22/26
Pupils unequal; knee reflexes hyperactive; tremors	Confused, disoriented and elated, with auditory hallucinations	Improved	Hospital
Speech defective; no other marked symptoms	Confused, disoriented, elated, overactive	Very much improved	Visit 6/17/26; discharged 6/17/27
Facial tremor; knee reflexes hyperactive; pupils rigid; speech defective	Confabulations; paranoid ideas; auditory hallucinations; emotional instability		Died 4/13/27
Pupils unequal, irregular; facial paralysis; general hyperreflexia; Rombergism	Elated; disoriented; grandiose ideas; memory defective; emotionally unstable	Very much improved	Visit 4/19/28
Pupils unequal, irregular, sluggish; general hyperreflexia; Rombergism; speech defective	Confused; no insight; steals in ward; wanders aimlessly; mischievous	Very much improved	Under consideration for visit
Pupils unequal, irregular, sluggish; knee reflexes hypoactive; tremors	Grandeur; apathy; polyphagia; confused; disoriented	Not improved	Hospital
Pupils unequal; knee reflexes unequal	Grandiose ideas; overactive; poor insight; psychomotor activity	Not improved	Deported 7/13/27
Pupils unequal	Grandiose ideas	Very much improved	Visit 3/18/27; discharged 3/18/28
Pupils unequal, irregular, sluggish; knee reflexes hyperactive	Disoriented; apprehensive; agitated; confused; confabulations	Very much improved	Under consideration for visit
No marked signs	Hallucinated; deluded; hyperactive; poor judgment	Very much improved	Visit 4/26/27; discharged 4/26/28
Pupils unequal, sluggish; knee reflexes absent; Rombergism	Retarded; deteriorated; visual hallucinations	Not improved	Hospital
Pupils unequal, irregular; knee reflexes hyperactive	Confused; no insight	Very much improved	Visit 12/24/26; discharged 12/24/27
Knee reflexes hyperactive; speech defective	Euphoria; auditory hallucinations	Very much improved	Visit 4/8/28
Pupils irregular, rigid; general hyperreflexia; Rombergism; speech defect	Visual and auditory hallucinations; ideas of persecution; delusions	Very much improved	Visit 11/1/27
Pupils rigid; speech defective; tendon reflexes hyperactive	Auditory hallucinations; disoriented; destructive	Improved	Hospital
Pupils irregular, sluggish; clonus of right knee; speech defective	Euphoria; grandeur	Very much improved	Visit 4/4/28
General hyperreflexia	Slightly confused; irritable; no insight	Not improved	Hospital
Tremors of hands and tongue; knee reflexes hyperactive	Disoriented, confused, deluded	Improved	Under consideration for visit when he escaped 5/29/28
Pupils irregular and rigid	Ideation slightly retarded	Not improved	Hospital
Pupils irregular; tendon reflexes hyperactive	Auditory hallucinations; accusatory delusions; no insight	Very much improved	Visit 6/15/27; discharged 6/15/28
Speech defective; general hyperreflexia of tendons	Grandeur; euphoria	Very much improved	Visit 4/9/28
Knee reflexes absent	Silly; partially disoriented	Aggravated; marked deterioration	Hospital
Pupils unequal, sluggish; tendon reflexes hyperactive	Auditory hallucinations; euphoria; grandeur; bizarre ideas; disoriented	Improved; was taken home against advice	Visit, 1/8/28; relapse; returned 5/1/28
Tremors of lips; pupils irregular, sluggish; hyperactive tendon reflexes	Grandeur; bizarre ideas; hard to manage in the ward	Not improved	Hospital
Pupils unequal, irregular, sluggish; knee reflexes absent	Accusatory ideas	Not improved	Hospital

TABLE 1.—*Analysis of 101*

Marginal Number	Case Number	Age and Sex	Date of Admission	Probable Date of Infection	Probable Date of First Symptoms	Date of First Chill	Date of Last Chill	Number of Chills	Serology *							
									Spinal Fluid Cell Count		Globulin Test		Wassermann Test		Colloidal Gold	
													Blood	Spinal Fluid		
									Before Treatment	After Treatment	Before Treatment	After Treatment	After Treatment	After Treatment	Before Treatment	After Treatment
72	37343	62-M	11/27/26	.....	.....	5/ 1/27	5/24/27	13	Normal	Normal	+	..	+	+	I	..
73	37869	38-M	10/13/27	.....	3 yr.	11/12/27	12/31/27	16	High	Normal	+	+	+	+	I	I
74	37617	35-M	5/10/27	.....	7 mo.	6/28/27	7/ 7/27	5	Normal	.....	+	..	..	..	I	..
75	36975	45-M	4/22/21	.....	1 yr.	8/ 1/25	8/17/25	14	Normal	Normal	+	+	+	+	I	I
76	37637	40-M	5/25/27	.....	2 yr.	7/ 9/27	7/11/27	3	Normal	Normal	+	+	—	—	I	I
77	37306	37-M	10/30/26	.....	2 yr.	12/ 3/26	1/ 1/27	14	High	.....	+	..	+	..	I	..
78	36959	47-F	2/23/26	.....	6 mo.	10/18/27	10/31/27	5	.....	.....	—	..	+	..	Flat	I
79	37284	42-M	10/ 6/26	.....	5 mo.	11/11/26	11/20/26	7	Borderline	Normal	—	+	+	—	I	I
80	36405	46-M	5/ 9/25	.....	.....	11/ 5/26	11/29/26	9	Normal	.....	+	..	—	..	I	..
81	31388	28-F	11/24/26	.....	.....	3/12/27	4/ 2/27	16	.....	Normal	..	+	+	..	..	I
82	36808	46-F	11/18/25	.....	.....	1/27/27	1/30/27	3	Normal	.....	+	..	..	..	I	..
83	37749	37-M	7/26/27	10 yr.	10 yr.	9/14/27	10/12/27	12	.....	Normal	+	—	+	+	I	I
84	37277	48-F	9/27/26	.....	1 mo.	11/ 4/26	11/ 6/26	9	High	.....	—	..	+	..	I	..
85	37274	32-M	9/22/26	12 yr.	12 yr.	10/ 7/26	11/ 5/26	13	Normal	Normal	+	+	+	+	I	I
86	37286	46-M	10/11/26	.....	15 mo.	11/13/26	11/18/26	6	.....	Normal	..	+	+	+	I	I
87	37784	32-M	8/22/27	.....	9 mo.	10/11/27	10/23/27	9	.....	.....	—	..	..	..	I	..
88	37658	44-F	6/ 6/27	.....	.....	10/13/27	11/ 2/27	13	High	.....	—	..	..	..	I	..
89	38026	34-M	1/23/28	.....	3 mo.	2/11/28	3/ 6/28	10	Borderline	Normal	+	+	+	+	I	I
90	25747	28-F	8/14/08	.....	.....	2/25/28	3/16/28	10	Borderline	.....	+	+	+	—	I	I
91	37992	40-M	12/31/27	13 yr.	10 mo.	2/25/28	7/25/28	1	Normal	Borderline	—	+	+	—	I	I
92	38077	35-M	2/26/28	9 yr.	6 mo.	3/19/28	4/ 4/28	11	Borderline	Normal	+	+	+	+	I	I
93	37971	36-F	12/13/27	12 yr.	1 mo.	2/ 8/28	3/ 7/28	3	Normal	Normal	+	+	+	+	I	I
94	38068	52-M	2/29/28	.....	1 yr.	3/21/28	4/ 5/28	9	Normal	Normal	+	+	+	+	I	I
95	38087	53-M	2/29/28	.....	7 mo.	3/30/28	4/16/28	13	Normal	.....	+	..	..	..	I	..
96	36273	35-M	3/19/25	.....	.....	.....	.....	0	Normal	.....	+	..	+	..	I	..
97	37985	70-M	12/ 8/27	.....	2 yr.	.....	.....	0	Normal	.....	+	..	+	..	I	..
98	38103	55-M	3/18/28	.....	3 yr.	4/ 4/28	4/25/28	10	High	.....	+	..	..	..	I	..
99	38139	41-F	4/11/28	.....	2 mo.	4/27/28	5/ 8/28	10	Normal	.....	+	..	..	..	I	..
100	38169	41-M	4/26/28	25 yr.	.....	5/16/28	5/30/28	15	Normal	.....	+	+	+	+	I	I
101	36470	32-M	6/ 9/25	.....	.....	10/19/25	11/14/25	18	High	Normal	+	+	—	+	I	I

Patients Treated—Continued

Neurologic Observations on Admission	Mental Status on Admission	Mental Status after Malarial Therapy	Present Status
Pupils unequal, rigid; knee reflexes hypoactive	Disoriented, overactive, resistive.....	Very much improved	Visit 2/4/28
Pupils rigid; tendon reflexes hyperactive; speech defective; gait unsteady	Euphoria; grandeur; no insight; memory and judgment poor	Improved.....	Hospital
Pupil rigid (one eye only present); speech defective; knee reflexes absent	Deterioration; grandeur	.....	Died 7/22/27
Knee reflexes absent; speech defect	Grandeur; psychomotor activity.....	Improved markedly..	Visit 6/15/28
Pupils irregular, rigid; speech defective	Grandeur; euphoria; no insight; poor memory	Improved.....	Hospital
Pupils unequal, irregular, rigid; knee reflexes hyperactive	Retardation; no insight; false perceptions	Not improved.....	Transferred to Tewksbury Infirmary 6/30/27
Pupils unequal; gait limping; hyperactive tendon reflexes	Retarded; difficulty in thinking; disoriented	Very much improved	Hospital
Pupils unequal, irregular, rigid; tremors of hands	Auditory hallucinations; paranoid reactions; grandeur	Not improved.....	Hospital
Pupils sluggish, irregular; speech defect; marked muscular incoordination; knee reflexes hyperactive; unable to stand	Auditory and visual hallucinations; exposes himself to physicians and nurses; masked face	Improved.....	Hospital
Pupils irregular, sluggish; knee reflexes hyperactive, unequal; speech defective	Disoriented; apathetic; irrelevant; deteriorated	Not improved.....	Hospital
Hyperactive tendon reflexes.....	Depression; persecutory and accusatory ideas; disorientation; poor judgment	Very much improved	Visit 7/10/27
Tendon reflexes hyperactive.....	Grandeur	Improved.....	Hospital
Tremors of hands.....	Auditory hallucinations; bizarre ideas....	Very much improved	Visit 12/4/26; discharged 12/4/27; committed suicide date undetermined
Knee reflexes hyperactive; tremors; speech defective	Euphoria; memory defective	Very much improved	Visit 2/11/27; discharged 2/11/28
Pupils rigid; knee reflexes unequal..	Grandeur; poor judgment.....	Improved.....	Hospital
Pupils sluggish; knee reflexes hyperactive; tremors; speech defective	Apathetic; indifferent; silly; deteriorated	Not improved.....	Deported 12/9/27
No marked signs.....	Restless; troublesome to other patients; disoriented; accusatory ideas	Very much improved	Visit 1/24/28
Pupils unequal, irregular, rigid; knee reflexes unequal; achillis reflex absent	Disoriented; grandiose and bizarre ideas..	Very much improved	Visit 6/29/28
Pupils sluggish; tendon reflexes hypoactive	Visual and auditory hallucinations; noisy; excited; irrelevant; talks to herself; silly	Not improved.....	Hospital
Pupils react poorly to light and distance; general hyperreflexia; Rombergism; speech defective	Grandeur; euphoria; persecutory delusions; no insight	Improved.....	Hospital
No marked signs.....	Grandiose ideas; confabulations.....	Very much improved	Visit 6/24/28
Facial paralysis	Disoriented; grandeur; no insight.....	Very much improved; relapsed	Visit 4/24/28; returned 5/26/28
Knee reflexes hyperactive.....	Auditory hallucinations; grandiose and bizarre ideas; restless	Not improved.....	Hospital
Knee reflexes hyperactive; pupils sluggish	Restless; steals other patients' belongings; grandiose ideas	.....	Died 4/19/28
No marked signs.....	Assaultive; indifferent; seclusive; hallucinated	Not improved.....	Hospital
Pupils irregular, rigid.....	Euphoric, chuckles to himself.....	Not improved.....	Hospital
Pupils sluggish; ankle clonus; knee reflexes absent	Noisy, excited, disoriented; speech defective; persecutory delusions	.....	Died 4/4/28
Pupils unequal, irregular, rigid; knee reflexes hypoactive	No insight; poor memory.....	Not improved.....	Hospital
Tremors; slurring speech; Rombergism; knee reflexes hyperactive; pupils irregular and rigid	Grandiose ideas; noisy, excitable, with periods of depression; restless; assaultive; disoriented	Not improved.....	Hospital
No marked signs.....	Restless, hysterical, resistive, depressed....	Not improved.....	Hospital

Jaundice.—Although jaundice is fairly common, the actual percentage of cases in which it occurred in this group has not been determined.

Cachexia and Anemia.—Cachexia and a certain degree of anemia appear together. Cachexia is to be expected in every case and usually is not alarming. Increasing the weight of the patients is practically within the control of the physician, for during or after the course of the elixir of iron, quinine and strychnine, N. F., for a month they regain normal weight, and in some cases even exceed it.

Ruptured Spleen.—Two cases of spontaneous rupture of the spleen were discovered. A more extensive report of these cases will be made in a subsequent article. In one of these, case 101, splenectomy was performed, and the patient made an uneventful recovery. Spontaneous rupture of the spleen should always be watched for, and operation should be resorted to as soon as it is discovered.

Cerebral Hemorrhage and Edema.—This condition occurred in case 95. The story was as follows:

> Three days after the thirteenth chill the patient, apparently without provocation, jumped through a window from the fourth story. Autopsy revealed hemorrhage and edema of the brain, in addition to an enlarged and ruptured spleen and fractured ribs. It is believed that the ruptured spleen and fractured ribs were incidental to the fall, and that the edema was the cause of the sudden maniacal episode.

SURGICAL OPERATIONS ON PARETIC PATIENTS

Surgeons in general hospitals are often reluctant to operate on a patient who has a positive Wassermann reaction of the blood, and visiting surgeons in state hospitals do not like to operate on paretic patients except in emergencies. These surgeons fear that the wound may fail to heal. The experience in the Worcester State Hospital is to the contrary. In the 101 cases reported in this series, nine patients had undergone surgical operations, which include herniorrhaphy, hemorrhoidectomy, tonsillectomy, unilateral herniorrhaphy, oophorectomy, repair of a simple fracture, repair of a compound fracture which later had to be followed by osteotomy and curettage and a repair of a fracture of the jaw. They made prompt and good recoveries. These figures do not include data for paretic patients outside of the series who have undergone surgical operations; these too had uneventful recoveries.

CONTRAINDICATIONS

I believe that the majority of paretic patients are suitable for this type of treatment. Students of the subject consider that patients who present one or more of the following conditions are unfit for malarial treatment: anemia, impaired renal function, jaundice, active pulmonary

lesion, debilitated condition, extreme old age, marked generalized arteriosclerosis, aortic aneurysm and functional or organic lesions of the heart.

SEROLOGY

In the analysis of these cases an effort has been made to compare the serologic observations before administration of malaria with those after the patient has recovered from the malaria, that is, within a few weeks and not exceeding six months after the last chill.

Cytology.—In describing the cytologic condition of the spinal fluid, I have adopted more or less arbitrary terms based on an accepted normal count of from 1 to 8 cells per cubic millimeter. I consider from 9 to 15 as borderline, and 15 or more as high. Table 1 shows the cell count

TABLE 2.—*Cell Count Before and After Treatment*

Before Treatment			After Treatment		
	No. of Cases	Percentage		No. of Cases	Percentage
High	25	28.7	High	2	3.6
Borderline	11	12.6	Borderline	1	1.8
Normal	51	58.6	Normal	52	94.5
Total	87		Total	55	

TABLE 3.—*Globulin Content of the Spinal Fluid*

Before Treatment			After Treatment		
	No. of Cases	Percentage		No. of Cases	Percentage
Positive	84	87.5	Positive	55	87.3
Negative	12	12.5	Negative	8	12.6
Total	96		Total	63	

before and after the treatment in each case. Table 2 is a summary of the cytologic condition before and after treatment.

Globulin.—When globulin is present before the administration of malaria, it almost invariably persists after the chills have been stopped. It may be concluded, therefore, that the globulin content of the spinal fluid is not affected by the paroxysms or the parasites at least for six months after the chills have been stopped. This is shown in table 3.

Wassermann Reactions of the Blood and of the Spinal Fluid.—Wassermann tests with the blood and spinal fluid were made soon after or within a few weeks after the chills. A small percentage gave negative results, which were due chiefly, I believe, to the other forms of antisyphilitic remedy administered to every patient as a follow-up treatment. It may, therefore, be inferred that the malaria does not affect materially the Wassermann reaction of the blood and spinal fluid. The results are given in table 4.

Colloidal Gold Test.—In studying table 1, it is apparent that very few changes in the colloidal gold curve take place after treatment. The zone 1 (paretic) curve almost invariably persists. Atypical zone 1 curves are found in only a few. It is fairly safe to conclude, therefore, as shown in table 5, that the colloidal gold curve is not affected.

CLINICAL RESULTS

The clinical results obtained in this series may be divided into six groups: (1) markedly improved; (2) improved but unfit for visit home or discharge; (3) unimproved; (4) aggravated; (5) relapsed; (6) died.

TABLE 4.—*Wassermann Reactions with Blood and Spinal Fluid After Treatment*

Blood			Spinal Fluid		
	No. of Cases	Percentage		No. of Cases	Percentage
Positive	61	81.3	Positive	58	84.0
Negative	14	18.6	Negative	11	15.9
Total	75		Total	69	

TABLE 5.—*Colloidal Gold Curve*

Before Treatment			After Treatment		
	No. of Cases	Percentage		No. of Cases	Percentage
Zone 1	93	96.8	Zone 1	61	92.4
Atypical zone 1	2	2.0	Atypical zone 1	3	4.5
Flat	1	1.0	Flat	2	3.0
Total	96		Total	66	

Group 1 includes patients whose mental and physical conditions justify recommendation for a visit home for a year, or for a discharge twelve months later if the condition no longer necessitates regular hospital supervision. This group includes thirty-three cases, or 32.6 per cent of all the patients treated.

Group 2 includes patients who on or soon after admission manifested marked psychotic symptoms that partially or completely disappeared after treatment, and who could be more easily cared for in the ward or could be given a parole on the hospital grounds. They were, however, unfit to be sent home on a visit. This includes sixteen cases, or 15.8 per cent.

Group 3 includes patients whose mental symptoms did not improve. There are thirty-two cases in this group, or 31.6 per cent.

Group 4 includes patients whose mental symptoms were apparently aggravated. This group includes only one case, or less than 1 per cent.

Group 5 includes patients whose mental symptoms were markedly improved and who were therefore sent home on a visit; there they suffered from a relapse later. There are only three cases in this group, or 2.9 per cent.

Group 6 may be conveniently divided into subgroup *A*, which includes deaths that resulted directly or indirectly from malaria, and subgroup *B* which includes deaths that resulted from other causes. Each subgroup includes eight cases, or 7.9 per cent.

Mortality.—The mortality rate from inoculated malaria is fairly low. Of the sixteen deaths recorded in this series, six occurred from six to twenty-eight months after the last chill; two occurred within two months after the last chill, and eight occurred within one month after the last chill. If the last eight deaths can be ascribed fully to malaria, directly or indirectly, the mortality rate in this series is about 8 per cent. Other workers, however, report a much lower mortality rate. Table 7

TABLE 6.—*Clinical Results Obtained from Malarial Therapy*

	Number of Cases	Percentage
Group 1 (improved markedly)	33	32.6
Group 2 (improved but unfit for visit)	16	15.8
Group 3 (unimproved)	32	31.6
Group 4 (aggravated)	1	0.9
Group 5 (relapsed)	3	2.9
Group 6: A (died directly or indirectly from malaria)	8	7.9
B (died from other causes)	8	7.9
Total	101	

presents an analysis of all the deaths in malaria-inoculated paretic patients in this series.

Present Status of Patients Now on Visit Home or Discharged.—Efforts have been made to determine the physical, mental and economic conditions of all the patients who are now on a visit home or have been discharged. A simple questionnaire was mailed to the guardians of these patients. When a reply was not obtained or when the letter was returned "unclaimed," social workers made a personal investigation. As a result, 85 per cent of these patients have been traced. Table 8 shows their present degree of health, and table 9 shows their economic status.

It may be of interest to mention that at the date of writing this paper the twenty-three patients referred to in table 9 who are working steadily are doing practically the same work as before they came to the hospital. Their present occupations include that of a clerk, canvasser, carpenter, housekeeper, painter, farm hand, automobile salesman, shipper in a bakery, mill operative, decorator and painter, jewelry salesman, leather worker and matron.

TABLE 7.—*Deaths Among Malaria-Inoculated Patients*

Marginal Number	Date of Last Chill	Date of Death	Time Interval	Anatomic Observations at Necropsy
4	1/ 9/25	1/11/26	2 days	No necropsy
14	1/22/26	5/18/28	27 months, 26 days	Bronchopneumonia; cerebral edema
16	7/19/26	7/24/26	5 days	Ruptured spleen
18	10/23/25	11/ 4/25	11 days	No necropsy
23	6/ 4/26	3/26/28	21 months, 21 days	No necropsy
25	12/ 4/25	10/25/26	10 months, 21 days	No necropsy
28	6/13/26	7/12/26	29 days	Lobar pneumonia and bronchopneumonia; enlarged spleen; syphilitic aortitis
29	9/ 4/26	9/ 9/27	12 months, 5 days	Bronchial hemorrhage; necrosis of bronchi
34	6/ 4/25	7/28/26	1 month, 24 days	No necropsy
37	12/24/26	6/26/27	6 months, 4 days	Asphyxia in an attempt to swallow a piece of meat; parenchymatous nephritis; infarcted spleen
43	8/13/26	6/16/27	10 months, 3 days	Suicide; fractures of femurs, sternum and cervical vertebrae; rupture of aorta and vertebral arteries
45	1/ 8/26	2/15/26	1 month, 7 days	No necropsy
49	3/21/27	4/13/27	12 days	No necropsy
74	7/ 7/27	7/22/27	15 days	No necropsy
94	4/16/28	4/19/28	3 days	Suicide; multiple fractures; ruptured spleen; cerebral hemorrhage
98	4/25/28	5/ 4/28	9 days	No necropsy

TABLE 8.—*Present Degree of Health of Patients Now on Visit or Discharged*

	Number of Cases	Percentage
In "excellent" health	11	33.3
In "good" health	14	42.4
In "fair" health	2	6.0
Died	2	6.0
Unaccounted for	4	12.1
Total	33	

TABLE 9.—*Present Economic Condition of Patients Now on Visit or Discharged*

	Number of Cases	Percentage
Working steadily	23	69.6
Not working	4	12.1
Died	2	6.0
Unaccounted for	4	12.1
Total	33	

SUMMARY

1. Malaria has caused marked improvement in 32.6 per cent of 101 patients treated, enabling them to be sent home on a visit or to be discharged.

2. About 16 per cent of the patients treated showed improvement, though they were as yet unfit for a visit home; 3 per cent had relapses.

3 Malaria has been given only in selected cases.

4. Malarial blood, from 4 to 8 cc., collected when the donor has a temperature of 104 F. or higher and given intravenously without delay, seems to give better results in that the incubation period is materially shortened.

5. The relationship between the clinical results and the number of paroxysms has not been established.

6. Cachexia developing in the course of inoculated malaria should not cause particular alarm.

7. Spontaneous rupture of the spleen should always be watched for, and splenectomy should be resorted to without delay when recognized.

8. Paretic patients may be operated on with reasonable assurance of prompt healing.

9. Approximately 60 per cent of the paretic patients who come to the Worcester State Hospital show a normal cell count of the spinal fluid; about 30 per cent have a high count, and approximately 10 per cent are on the borderline. After the administration of malaria, practically all patients show a normal cell count.

10. Approximately [illegible]nt of the paretic patients admitted to the Worcester State Hosp[illegible]ow globulin in the spinal fluid. There are practically no changes in the globulin reaction after treatment with malaria.

11. Twenty per cent of the Wassermann reactions of the blood are negative after treatment with malaria.

12. Sixteen per cent of the Wassermann reactions of the spinal fluid become negative after treatment with malaria. However, all these patients receive antisyphilitic treatments subsequent to the malaria.

13. The colloidal gold curve is slightly, if ever, affected.

14. A relationship between the serologic changes and the clinical improvement has not been fully established.

15. The mortality rate due to inoculated malaria, directly or indirectly, is 7.9 per cent.

16. Of the thirty-three patients now on a visit home or discharged, 33.3 per cent are in "excellent" health; 42.4 per cent are in "good" health, and 6 per cent are in "fair" health.

17. Of the group now at home on a visit or discharged, 70 per cent are working steadily.

CONCLUSION

Malaria is of great value as a therapeutic agent in paresis. It has caused a marked improvement, resulting in a visit home or discharge in about 33 per cent, and a limited improvement in about 16 per cent of the patients treated. It deserves a trial in every case of paresis in which the physical condition does not contraindicate its administration.

The author is indebted to Dr. R. T. Draper, formerly a member of the staff of the Worcester State Hospital, who conducted the early phase of this work and who was responsible for the inoculation with malaria of the first fifty patients in this series.

SPECIAL ARTICLE

ETIOLOGY OF EPIDEMIC ENCEPHALITIS

ITS RELATION TO HERPES, EPIDEMIC POLIOMYELITIS AND POST-VACCINAL ENCEPHALOPATHY *

C. LEVADITI

Head of Department of Microbiology, Pasteur Institute; Member of the Academy of Medicine

PARIS, FRANCE

ETIOLOGY AND PATHOGENESIS OF EPIDEMIC ENCEPHALITIS; ITS RELATION TO HERPES

No problem has given rise to so much activity or to so many publications as that of the etiology of epidemic encephalitis. It is not my intention to make a complete bibliographic survey of the question, nor would this be in harmony with the spirit of the work undertaken by the Matheson Foundation. I shall give, as briefly as possible, a summary of my own researches, in order to uphold, by the aid of definite and unimpugnable experimental facts, my present conception of the etiology and pathogenic mechanism of von Economo's disease.

At present, one main idea dominates the problem of the etiology of epidemic encephalitis, and that is the relation between the virus of herpes and the filtrable virus which is regarded as the causative agent of von Economo's disease. It seems necessary, therefore, to explain this idea in detail, following step by step the development of the experimental researches undertaken since 1920.

Harvier and I [1] were the first to isolate from the brain of an encephalitic subject an ultravirus pathogenic for the rabbit, capable of being maintained by successive passages through that animal. We were also the first to define most of the properties by which this virus can be identified and to study not only the pathologic histology of the experimental lesions, but also the pathogenic mechanism of encephalitis.

The researches of Strauss, Hirshfeld and Loewe,[2] and of McIntosh and Turnbull,[3] which preceded by a short time the initial work of

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1. Harvier, P., and Levaditi, C.: Compt. rend. Soc. de biol. **83**:354, 1920; Ann. de l'inst. Pasteur **34**:911, 1920. Levaditi, C.; Harvier, P., and Nicolau, S.: Ann. de l'inst. Pasteur **36**:63, 105, 1922. Levaditi, C.: Les ectodermoses neurotropes, Paris, Masson & Cie, 1922.

2. Strauss, I.; Hirshfeld, S., and Loewe, L.: New York M. J. **109**:772, 1919; J. Infect. Dis. **25**:378, 1919.

3. McIntosh, J. A., and Turnbull, H. M.: Brit. J. Exper. Path. **1**:89, 1920.

Harvier and myself, are by no means equal in identical value to our observations. The American scientists did not have at their disposal an encephalitic virus of sufficiently constant virulence to allow of a systematic examination of the problem. Most of their strains were derived from nasopharyngeal secretions of subjects suffering from von Economo's disease, i. e., from a medium which might contain numerous other viruses, notably the virus of herpes (Levaditi, Harvier and Nicolau, Doerr and Schnabel). No experiment on cross-immunity between these strains and the herpetic virus has been reported, however, by Strauss and his collaborators, so that they have yet to be identified. If one considers further the fact that the workers at Mount Sinai Hospital have readily cultivated their viruses on the Smith-Noguchi medium —which no other experimenter has been able to confirm—one will realize with what caution these data must be accepted.

The same caution is necessary in connection with the initial researches of McIntosh and Turnbull on the transmission of epidemic encephalitis to the monkey. These scientists inoculated *Cercopithecus pathas* with material (neuraxis) derived from an encephalitic subject (Derby epidemic) and seem to have caused a disease leading to delayed death (after two months); this condition was characterized by lesions resembling those of von Economo's disease. The experiment seemed to prove that the virus of encephalitis is pathogenic for the simian species. On the other hand, it is now known that the filtrable virus isolated by Harvier and myself and by the investigators who have confirmed our work has the peculiarity of being rarely virulent for the monkey.

For these reasons, I think it fair to regard the experiments of Harvier, Nicolau and myself as being the first to place the problem of the etiology of von Economo's disease on a strictly scientific basis. The essential facts brought out by these experiments may be considered. Harvier, Nicolau and I have established; inter alia, the following facts:

1. When laboratory animals (*catarrhina* monkeys, rabbits, guinea-pigs, mice and other animals) are inoculated with encephalitic material by the most various routes (blood, cerebrospinal fluid, nasopharyngeal secretions, substance of nerve centers), it is surprising how seldom positive results are obtained. Despite innumerable attempts, only two strains of virulent organisms (one from the neuraxis and the other from the nasal secretions) have been isolated. A third strain proved to be only slightly pathogenic.

2. Direct transmission of the virus from man to animal has been secured only in the rabbit. It is a curious fact that if several rabbits are given cerebral injections of material from a human being only one animal will contract encephalitis, while the others will remain entirely free

from infection. Nevertheless, the latter are not immune to the virus, for if they are subsequently reinfected with the same original strain, they will contract fatal encephalitis.

3. When, owing to circumstances which I shall mention later, the transmission of the encephalitic virus to the rabbit is successful, the maintenance of the virus by regular passages through animals of the same species becomes easy. Like the rabic virus or the filtrable virus of poliomyelitis, the encephalitic virus can be inoculated in series, cerebrally or otherwise.

4. Once a fixed strain was obtained, it was relatively easy to undertake an experimental study, both etiologic and pathogenic, of von Economo's disease. Several points have been cleared up, such as the characteristics of the encephalitic virus, the clinical and anatomopathologic aspect of the infection in the various receptive species, the routes by which the virus penetrates, its distribution in the organism, how it is eliminated, immunity, the problem of germ carriers and other points. These questions are fully dealt with in the monographs entitled "Les ectodermoses neurotropes" [4] and "L'herpes et le zona." [5]

The problem of the etiology of von Economo's disease seemed thus to be solved when a new fact came to light which entirely changed its aspect and opened the way for fresh research.

Guided by the embryogenic conception of the tissue affinities proper to certain ultraviruses belonging to the neurotropic ectodermatosis group, Harvier and I [6] tested the virulence of the encephalitis virus for the cornea, a segment of the ectoderm which is extremely receptive to vaccine. Was the encephalitic virus keratogenous? In other words, was it capable of producing a keratitis similar to vaccinal keratitis? If so, would that virus be able to infect the neuraxis along the nerve tracts connecting the cornea with the mesencephalon and the medulla oblongata? Harvier and I [7] had previously shown that the virus of von Economo's disease when introduced into the anterior chamber of the eye infected the encephalon by the retinal and optic routes. Would the same result be obtained by inoculating this virus into the cornea after scarification?

The experimental results were highly illuminating. After from twenty-four to forty-eight hours' incubation, rabbits infected by corneal scarification showed the beginning of a keratitis accompanied by seropurulent conjunctivitis. Opacification of the cornea was progressively accentuated, and in due course a genuine parenchymatous keratitis

4. Levaditi, C. (footnote 1, fourth reference).
5. Levaditi, C.: L'herpes et le zona, Paris, Masson & Cie, 1927.
6. Harvier, P., and Levaditi, C.: Compt. rend. Soc. de biol. **84**:300, 1921.
7. Harvier, P., and Levaditi, C.: Compt. rend. Soc. de biol. **83**:1140, 1920.

appeared, which invaded the whole of the tissue and was accompanied by symptoms of iritis. The process, however, was not confined to the cornea. After from eight to twelve days' incubation, all of the animals showed neurotic disturbances pointing to an invasion of the neuraxis by the encephalitic virus. In general, these disturbances recalled those observed after subdural inoculation: paresis, convulsions, myoclonic movements, somnolence, salivation and "mouvements de manège." Most of the rabbits succumbed after a few days' illness, and histologic examination of the encephalon revealed the characteristic alterations of encephalitis in man and experimental encephalitis (monocytic meningitis, perivascular cuffs, parenchymatous inflammation with polymorphonuclears). Here and there were degenerative modifications of the basal cortex and Ammon's horn (elective zone of Levaditi, Harvier and Nicolau) and also symptoms of neuronophagy. These alterations, however, were less pronounced than in animals in which encephalitis was produced by the introduction of virus into the brain (in certain rabbits the infection was more chronic, but it was always fatal).

The conclusion to be drawn from these experiments, and the only conclusion warrantable at the time, was that the encephalitic virus of Levaditi and Harvier had no single exclusive neurotopism. Apart from its neurotic affinities, which had already been established, this virus was capable of attacking other segments of the ectoderm, particularly the cornea and the epidermis.

All this happened in February, 1921. As early as 1913, however, a group of the foremost German research workers had engaged in the experimental study of herpes, and had arrived at conclusions of the highest theoretical and practical importance.

Grüter,[8] a true pioneer, had shown that the herpetic keratitis of man (the so-called dendritic keratitis) was transmissible to the rabbit. Inoculation of the cornea of this animal with matter derived from corneal herpes in man produced a typical keratitis transmissible in series and leaving, after cure, a state of specific local immunity. These researches, confirmed by Kraupa,[9] were taken up by Löwenstein[10] (of Prague), who extended them to cutaneous and mucous herpes. Löwenstein showed that not merely corneal herpes, but also simple herpes and symptomatic herpes accompanying pneumonia, cerebrospinal meningitis or tuberculosis can be inoculated into the cornea of the rabbit; inoculation causes the appearance of a specific keratitis transmissible from animal to animal. From this the conclusion was drawn

8. Grüter: Arch. f. Augenh. **70**:241, 1911-1912; Ber. ü. d. Versamml. d. ophth. Gesellsch. **42**:162, 1920.

9. Kraupa: München. med. Wchnschr. **67**:1236, 1920.

10. Löwenstein: München. med. Wchnschr. **66**:769, 1919; Klin. Monatsbl. f. Augenh. **64**:15, 1920.

that herpes was a specific infectious disease produced by a virus which was probably invisible and filtrable, and which was virulent for the rabbit.

The question would have been left at that point, and would not have been transferred from the domain of ophthalmology and dermatology to that of neurology had not a fresh discovery, the importance of which cannot be overestimated, supplemented the knowledge on this subject. I refer to the neurotropism of the herpetic virus which was established by Doerr and Vöchting.[11] In October, 1920 (seven months after our first study of the encephalitic virus and four months before Harvier's and my note on encephalitic keratitis), the Swiss scientists stated that in rabbits suffering from herpetic keratitis they had observed general disturbances pointing to an invasion of the nerve centers by the virus of herpes. These disturbances resembled those presented by our encephalitic rabbits.

It followed from this that the virus of herpes did not restrict itself to the cornea. Through channels which had still to be ascertained, it invaded the central nervous system, where it multiplied and produced lesions, thus occasioning a characteristic neuraxic syndrome. The herpetic virus, therefore, was not only dermotropic but neurotropic, at least in the rabbit experimentally inoculated by the corneal route.

Any investigator familiar with the researches of Harvier, Nicolau and myself on the encephalitic virus and with the discoveries of Grüter, Löwenstein and Doerr in connection with the virus of herpes would have been tempted to see a close kinship between these two viruses, although their sources are so different and apparently so widely separated. I must confess that this did not occur to me for the simple reason that, being absorbed in the study of encephalitis, I had entirely ceased to think about any other subject.

This idea of kinship, however, was seized on by other investigators, and has led to the fundamental conception referred to at the beginning of this article—that of the identity in nature of the virus of encephalitis and the virus of herpes. How and by whom was this discovered?

One frequently reads in German papers that the analogy between the virus of von Economo's disease and that of herpes was first realized by Doerr and his collaborator Vöchting. Nothing could be further from the truth. It is to Blanc, director of the Pasteur Institute at Athens, that the credit is due for having been the first to call attention to the analogy between the properties of the encephalitic virus isolated by Harvier and myself and those of the virus of herpes. In a paper submitted to the Academie des Sciences[12] in March, 1921,

11. Doerr and Vöchting: Rev. gén. d'opht. **34**:409, 1920.
12. Blanc: Compt. rend. Acad. d. sc. **172**:725, 1921.

Blanc, having verified the observations of Grüter, Kraupa and Löwenstein regarding the possibility of inoculating the virus of herpes into the rabbit, having established certain new facts and having demonstrated, after Luger and Lauda, that the virus is filtrable, reproduced our observations on the encephalitogenous keratoconjunctivitis caused by the virus of von Economo's disease. The resemblance is so striking that it could not escape alert observers. Blanc realized its full importance, and concluded thus:

> All these properties can be superimposed on those found by Levaditi and Harvier in the virus of epidemic encephalitis. The fact that in my experiments I obtained a weaker virulence by scarification of the cornea seems to constitute a distinction between these viruses. This difference may be due to a greater neurotropism acquired by the virus of epidemic encephalitis—a property which our virus will perhaps acquire by passages on the encephala of rabbits.

The relationship has been established. Henceforth, one will have to reckon with this resemblance in nature, clinical symptoms and anatomopathologic lesions between the virus of encephalitis and that of herpes, notwithstanding the caution—even the doubt—with which the systematic mind, stored with acquired knowledge, will receive this "revolutionary" conception. Investigators will undertake research in order to establish whether there is a true identity between these viruses, and whether herpes and encephalitis are identical from the etiologic point of view.

This was done without delay by Doerr and Schnabel [13] at Basle, and by Harvier, Nicolau and myself [14] at the Pasteur Institute at Paris. The plan of research was extremely simple—to make a comparative study of the virus of encephalitis and that of herpes, with reference to their properties in general, and especially with reference to cross-immunity. If the virus of one of these conditions vaccinates the cornea and the neuraxis against the other, that means that they are more or less identical, and that von Economo's disease and herpes have a common etiology. If, on the other hand, the virus does not confer immunity to the other disease, that means that, as in rabies, poliomyelitis and encephalitis (Levaditi, Harvier, Nicolau and Amoss [15]), the viruses are not similar.

Doerr and Schnabel [16] were the first to report such experiments on cross-immunity. They established the fact that if rabbits inoculated through the cornea with the virus of herpes survived the infection, they could resist a corneal and intradural inoculation with encephalitic virus (Basle I strain) which is fatal to animals that have not been

13. Doerr and Schnabel: Schweiz. med. Wchnschr. **2**:469 and 562, 1921.

14. Harvier, P.; Nicolau, S., and Levaditi, C.: Compt. rend. Soc. de biol. **85**:213, 1921.

15. Amoss, H.: J. Exper. Med. **33**:187, 1921.

16. Doerr and Schnabel: Ztschr. f. Hyg. u. Infectionskrankh. **94**:29, 1921.

inoculated previously. Conversely, animals which survive an encephalitic keratitis are immunized locally (cornea) and generally (brain) to the virus of herpes, which is virulent for control rabbits. Consequently the two viruses are identical.

Harvier, Nicolau and I, having at our disposal only the encephalitis virus, were unable to undertake such experiments until after Doerr and Schnabel had done so. Their principal results are as follows:

> All the researches undertaken with the hepatic virus (Blanc strain) have shown that this virus is not distinct from the virus of encephalitis (Levaditi and Harvier strain); the only difference between the two viruses is one of virulence, the virus of herpes having as a rule a less marked pathogenic activity than that of encephalitis.
>
> They are equally filtrable, can be equally well preserved in glycerine and in the dry state, and produce the same symptoms in animals inoculated by the ocular or the cerebral route. Moreover, the histopathologic lesions are absolutely identical. This identity is also proved by the researches into cross-immunity: the virus of herpes vaccinates the cornea against the fixed virus of encephalitis and the virus of healthy carriers. Conversely, animals which, as the result of successive corneal inoculations, resist the keratogenous and encephalitic salivary viruses, are immunized to the virus of herpes.[17]

The relations between the two viruses seem still closer when one considers their affinity for the cutaneous segment of the ectoderm. In this connection, experience shows that the filtrable virus of herpes, taken direct from man or after numerous passages through the rabbit, is, like the encephalitic virus, endowed with marked cutaneous affinities. To judge by the intensity and the evolution of herpetic lesions of the skin in the rabbit, the ectodermatotropic affinities of the herpetic virus exceed those of the virus of von Economo's disease. There is thus a certain contrast between the cutaneous (dermatotropic) and the cerebral (neurotropic) affinities of these viruses, and this may be expressed by the following formula:

	Cutaneous Affinity	Cerebral Affinity
Encephalitic virus	+	++++
Herpetic virus	++++	++

These observations, taken as a whole, gave an unforeseen aspect to the problem of the etiology of epidemic encephalitis. This led to an important conception (mentioned at the beginning of this article) arising out of the identity in nature of the virus of encephalitis and that of herpes; it may be summarized thus:

> In certain subjects the nasopharynx and the saliva contain a specific filtrable virus, the virulence of which varies within fairly wide limits. The principal varieties of this virus behave toward one another like more or less virulent strains

17. Extract from Levaditi's monograph: Les ectodermoses neurotropes, Paris, Masson & Cie., 1922.

of certain cultivable organisms such as the streptococcus, the meningococcus or the pneumococcus. Except in epidemic periods, the salivary virus produces in these subjects only transitory disturbances or local affinities of little importance, with or without effects on the general system, such as herpes simplex, herpes febrilis, herpetic tonsillitis, herpes of the cornea, etc. Sometimes the infectious process reaches the nervous system, in which it produces neuralgic pains (Mauriac's neuralgic herpes), a certain meningeal irritation and spinal lymphocytosis (Ravaut and Darré[18]). In other persons—the majority—the virus vegetates in the nasopharynx without betraying its presence by the slightest symptom.

At some moment, owing to an increase in its virulence, the salivary virus acquires the property of attacking the central nervous system. Originally epitheliotropic, it now becomes plainly neurotropic. It endeavors to pass the barrier presented by the nasopharyngeal mucous membrane in order to approach the neuraxis along the nervous tracts. If the barrier gives way owing to a common inflammatory alteration of the mucous membrane, the virus invades the encephalon and produces von Economo's disease.

Thus the salivary virus, the virus of herpes and the virus of encephalitis are ultimately only variants, with unequal pathogenic potency and progressively increasing neurotropism, of one and the same filtrable virus, the encephalitogenous ultravirus (Levaditi).

This etiologic conception of epidemic encephalitis was subjected to control research. It was questioned whether the virus isolated by Harvier and myself really came from cases of encephalitis in man or whether perhaps some error had crept into the investigations. In particular, there was thought to be a possibility of a spontaneous encephalic infection of the rabbit or an accidental herpetic contamination. These objections can easily be refuted, for the following reasons:

At the beginning, early in January, 1920, and throughout the period (more than a year) during which the researches of Harvier, Nicolau and myself were pursued, no experiment on the transmission of herpes to the rabbit was undertaken in our laboratory. Thus the hypothesis of contagion between experimental animals cannot be entertained. Further, suppose that the rabbit was capable of spontaneously contracting a disease of the herpetico-encephalitic type, keratogenous, encephalitogenous and with characteristic lesions of the neuraxis; this spontaneous disease would then appear in animals inoculated with material that would be avirulent, and, once started, it could be transmitted serially. The hypothesis is plausible, but there are no facts to confirm it.

After all, it would be surprising that the rabbit should be the prey of a latent infection resembling in all its features the herpetic disorder produced by inoculation with herpes irrespective of its clinical peculiarities or its origin. Moreover, consider the incalculable number

18. Ravaut and Darré: Ann. de dermat. et syph., June, 1904.

(hundreds of thousands) of subdural inoculations carried out on the rabbit in different countries with all sorts of viruses, especially that of rabies; how is it that spontaneous encephalitis of the herpetic type has not been reported during the course of these experiments?

Finally it is now known that the rabbit is subject to a contagious neuraxic infection to which the name of epizootic encephalomyelitis has been given, but both in clinical symptoms and in etiology this infection differs from the encephalitis produced by the filtrable herpetico-encephalitic virus.

For all these reasons, the hypothesis of the nonhuman origin of the virus first isolated by Harvier and myself must be definitely discarded.

The control researches reported since 1920 may be divided into two groups. Certain authors, proceeding experimentally, have isolated viruses producing in animals diseases different from those observed by us. They have therefore failed to confirm our researches. Others have fully verified our observations.

NONCONFIRMATORY RESEARCHES

Mention must first be made of the virus of Bastai,[19] isolated by inoculating encephalitic material from man into the rabbit and the cat. This virus is different from the herpetico-encephalitic strain of Harvier and myself in the symptomatology of the experimental disease, and also in the fact that when inoculated corneally into the rabbit it does not produce keratitis. My co-workers and I have had an opportunity of testing Bastai's researches in our own laboratory and in his presence; we found that the supposed filtrable virus isolated by him was in reality a cultivatable organism presenting most of the characteristics of the pasteurellosis of the rabbit. Bastai, therefore, was working with nerve centers secondarily infected, and was transmitting to his animals a purulent microbic meningitis followed by septicemia, which caused death after from twenty-four to forty-eight hours' incubation. Our observations, moreover, have been confirmed by Schnabel.[20] This observer in turn showed that the supposed encephalitic virus of Bastai, when inoculated cerebrally into the rabbit, kills the animal in from twelve to twenty-four hours, with concomitant meningitis. Positive brain cultures are obtained; the organism isolated resembles the coccobacillus. Corneal scarification produces a conjunctivitis and sometimes a mild keratitis, but the latter is different from the herpetico-encephalitic keratitis; it is fatal in from two to four days. Moreover, rabbits enjoying marked herpetic immunity are receptive to Bastai's virus.

19. Bastai: Riv. ital. di clin. med., April, 1920.

20. Schnabel: Klin. Wchnschr. **3**:1015, 1924.

Consequently, there is an error of interpretation at the bottom of Bastai's experimental researches, and these are not relevant to the etiologic study of von Economo's disease.

The observations of Ottolenghi, Tonietti and d'Antona [21] are almost contemporary with our own. They concern the positive inoculation of cerebrospinal fluid and blood from encephalitic patients (thirteen cases) into guinea-pigs, intracranially and peritoneally. Sometimes the animals presented signs of somnolence and succumbed in from five to thirty-five days after the injection. The brain was virulent for their own species and for the cat. The experimental disease was almost invariably fatal, only 13 of 255 guinea-pigs inoculated surviving. Cerebrospinal fluid from man would seem to be infectious on instillation into the nasal fossae; the virus was apparently present in the naso-pharyngeal secretions of sufferers from von Economo's disease.

It has thus been demonstrated that the observations of the Italian writers are in no way relevant to the investigations of Harvier and myself, Ottolenghi's virus being totally different from the encephalitogenous virus isolated at the Pasteur Institute. None of the authors who have had to deal with the etiology of epidemic encephalitis has confirmed these observations. Moreover, Ottolenghi and his collaborators observed in their animals only common neuraxic lesions: hyperemia, hemorrhage, and here and there degeneration of the neurons, but never the microscopic alterations characteristic of encephalitis in man. I should not be surprised if in this particular case, as in many others, the disease was in reality a spontaneous infectious disease of the guinea-pig produced by a filtrable virus and similar to the disease studied by Ionesco-Michaesti.[22]

More important, because richer in facts, are the studies of the Swedish school, undertaken in 1921 by Kling and his collaborators, Davide and Liljequist.[23]

These writers, during the course of an epidemic of encephalitis in Lapland (Sweden), undertook experiments with the object of verifying the observations of Harvier, Nicolau and myself. At first their experiments appeared to be confirmatory. Later, however, the problem changed aspect. They succeeded in producing encephalitis in the rabbit by inoculating encephalitic material (neuraxis, cerebrospinal fluid, filtered fecal matter) from cases in human beings, some of which were fatal. They themselves, however, soon realized that

21. Ottolenghi, D.; Tonietti, F., and d'Antona, S.: R. Accad. d. fisiocrit in Siena, February, 1920; Policlinico **27**:1075, 1920.

22. Ionesco-Michaesti: Compt. rend. Soc. de biol. **84**:1014, 1921.

23. The work of these authors, most of which was published in the Comptes rendus des séances de la Société de biologie, is to be found in the communications of the Laboratoire Bacteriologique de l'État Suedois, 1923, vol. 7.

the experimental disease differed greatly from that studied by my collaborators and myself. Whereas rabbits inoculated with the herpetico-encephalitic virus succumbed within a few days of inoculation, animals infected with the Swedish virus did not die for some weeks or even several months; most frequently neither death nor illness occurred. The success of the experiment in this case was proved only by the anatomopathologic lesions found in the neuraxis of rabbits killed long after inoculation. Moreover, these lesions presented an entirely different appearance from that of the alterations produced by the herpetico-encephalitic virus. They were not meningeal, vascular and parenchymatous modifications of a pronouncedly acute character, as is always the case in true encephalitis, but chronic lesions (meningitis with mononuclears, perivascular cuffs with monocytes and, above all, nodules or granulomas with epithelioid and giant cells).

The virus did not produce keratitis followed by encephalitis. Although it appeared to be capable of passing through the filter bougie like the herpetico-encephaltic virus, this virus showed numerous distinctive peculiarities. The action of heat, in particular, demonstrated that this virus resisted temperatures which completely destroyed the activity of the micro-organism isolated by us.

The reader wishing to familiarize himself with the question will find in the issue of the *Annales de l'Institut Pasteur* for August, 1924,[24] a memorandum dealing with the true nature of the Swedish virus. This article contains the arguments which gradually led my co-workers and me to identify the disease observed in the rabbit by Kling and his collaborators with an epizootic encephalomyelitis, reported from the United States and England by Bull,[25] Oliver,[26] and Twort and Archer.[27] The Swedish writers inoculated their animals with material of human origin, but von Economo's disease did not occur. The animals had in their systems the virus of epizootic encephalomyelitis, which they acquired by contact; subsequently, owing to the inoculation, they developed a chronic infection with a cerebral or renal localization.

Following the preliminary researches of Doerr and Zdansky,[28] and in particular the work of Nicolau, Schoen and myself,[29] it was found

24. Levaditi, C.; Nicolau, S., and Schoen: Ann. de l'Inst. Pasteur **38**:651, 1924.

25. Bull, C.: J. Exper. Med. **25**:557, 1917.

26. Oliver: J. Infect. Dis. **1**:91, 1922.

27. Twort, C. C.: Vet. J. 1922, vol. 78. Twort and Archer: Lancet **1**:1102, 1923.

28. Doerr and Zdansky: Schweiz. med. Wchnschr. **4**:349, 1923; Ztschr. f. Hyg. u. Infectionskrankh. **101**:239, 1923.

29. Nicolau, S.; Schoen, and Levaditi, C.: Compt. rend. Acad. d. sc. **177**: 985, 1923; Compt. rend. Soc. de biol. **89**:984 and 1157, 1923; **90**:194 and 662, 1924; Compt. rend. Acad. d. sc. **178**:256, 1924.

possible to establish definitely the nature and characteristics of the virus which produces spontaneous encephalopathy in the rabbit. So far from being invisible and filtrable, this virus can be readily detected, and is relatively easy to discover in sections and slides of brain and kidney. My collaborators and I have given it the name of *Encephalitozoon cuniculi*. It is a *Microsporidium*, a protozoon belonging to the subclass of the *Neosporidia*, order of *Haplosporidia*. The epizootic disease of the rabbit (and also of the mouse) is therefore a microsporidiosis. This is the first time that anyone has demonstrated the existence in mammals of a microsporidium similar to the *pébrine* of silkworms, to *Glugea lophii*, the neuraxic parasite of *Lophius piscatorius* (Doflein) and to the microsporidium of the grass snake (*Glugea danilewskyi*) studied by Guénot and Naville.[30] I may add that the disease is transmitted by contact, as the urine contains spores which produce contamination by soiling the food. The organism observed in 1922 by Wright and Craighead [31] in small rabbits suffering from an epizootic infectious motor paralysis, will in the future be known as *Encephalitozoon cuniculi* (Wright and Craighead, nov. spec.).

The same confusion concerning the epizootic encephalitis of the rabbit has crept into the work of Thalhimer,[32] and probably also into that of Strauss, Hirshfeld and Loewe.[2] Thalhimer endeavored to transmit encephalitis to the rabbit and, in contrast to what had been found at the Pasteur Institute and elsewhere, he succeeded in doing so in a large number of cases (100 per cent with human neuraxis, 85 per cent with cerebrospinal fluid, 100 per cent with nasopharyngeal secretions). These almost constant successes in themselves brought the results under some suspicion. I had, however, an opportunity of making a closer study of the so-called encephalitic virus of Thalhimer and succeeded in identifying it with the virus which causes the spontaneous disease of the rabbit. It was, in fact, simply *Encephalitozoon cuniculi*, the presence of which was demonstrated both in the brain and in the kidney of the experimentally infected animals.

CONFIRMATORY RESEARCHES

The ground was accordingly cleared of what Bastai, Ottolenghi and his collaborators, Kling, Davide and Liljequist, Thalhimer and, up to a certain point, Strauss and the workers at Mount Sinai Hospital each regarded from his own point of view as the true etiologic agent of von Economo's disease. Our researches remained, proving that the

30. Guénot and Naville: Rev. suisse d. Zool., 1922, vol. 30.

31. Wright and Craighead: J. Exper. Med. **36**:135, 1922.

32. Thalhimer, W.: Encephalitis, Cultural and Experimental Studies, Arch. Neurol. & Psychiat. **5**:113 (Feb.) 1921; Epidemic Encephalitis, ibid. **8**:286 (Sept.) 1922.

only virus of human origin isolated from the brain or nasopharyngeal secretions possessed all the characteristics of the herpetic germs. What was the later history of these researches? Were they subsequently confirmed? Did other investigators succeed in detecting the herpetico-encephalitic virus in the encephelon or in the cerebrospinal fluid?

Several students, both in France and elsewhere, have transmitted encephalitis to the rabbit, thus producing a disease due to a virus in every way comparable with the virus of Levaditi and Harvier. The strains isolated are few, particularly in proportion to the large number of experiments made. They can therefore easily be enumerated.

Encephalitic Strains, Herpetic Type, Isolated up to the Present Time.—(*a*) Levaditi and Harvier strains, of cerebral and nasopharyngeal origin.—Their principal characteristics have been confirmed by Schnabel.[20]

(*b*) Doerr and Schnabel strain (Basel I [1]).—The cerebrospinal fluid of an encephalitic patient (characteristic symptoms but no microscopic test) was inoculated cerebrally into the rabbit in a dose of 0.2 cc. The animal showed encephalitic symptoms on the fifth day and died on the sixth. Cerebral passages were positive (the animals succumbed between the fourth and eighth days). The strain is virulent for the guinea-pig and the mouse. The brains of the infected animals when inoculated into the cornea of the rabbit are found to be keratogenous. Fifteen per cent of the animals suffering from keratitis have neuraxic localizations. Identity with the herpetic virus has been demonstrated by cross-immunity.

(*c*) Doerr and Berger strain (Basel II [33]).—The case was one of epileptiform epidemic encephalitis, diagnosed as such by microscopic examination. The neuraxis was inoculated cranially into three rabbits. One of them presented nervous symptoms after eight days' incubation, and succumbed with typical lesions. The strain is keratogenous and can be maintained by successive passages. Identity with the herpetic virus has been demonstrated by cross-immunity.

(*d*) Berger strain (Basel III [34] and Zdansky [35]).—The patient was a woman, aged 32, with epidemic encephalitis of athetotic epileptic form, which was diagnosed anatomically. Postmortem examination revealed softening of the cerebral cortex, a scattering of punctiform hemorrhages, and, histologically, perivascular cuffs and a monocytic infiltration of the meninges. Inoculation of fresh brain into the rabbit gave no result; but subdural injection of glycerinated encephalon (fourteen days) led to encephalitis after from five to six days' incuba-

33. Doerr and Berger: Schweiz. med. Wchnschr. **3**:862, 1922.

34. Berger: Wien. klin. Wchnschr. **35**:801, 1923.

35. Zdansky: Frankfurt. Ztschr. f. Path. **29**:207, 1923.

tion. Passages were positive. The strain is keratogenous. Cross-immunity demonstrated the identity of this strain with the herpetic virus.

(*e*) Schnabel strain (Berlin [36]).—Cerebrospinal fluid was obtained in a case of acute encephalitis. The sediment obtained by centrifugating was inoculated cerebrally and corneally into several rabbits. One of the animals developed encephalitis seven days after inoculation. The virus is keratogenous and confers immunity against herpes; conversely, the herpetic virus immunizes against Schnabel's encephalitic strain.

(*f*) Luger and Lauda strain (Vienna [37]).—Cerebrospinal fluid from a fatal case of typical encephalitis was injected intravenously. (No histologic test was made. An endothelioma of the dura mater was present, on which the encephalitis supervened.) The rabbit inoculated showed nervous symptoms eighteen days after injection, and succumbed without apparent cerebral lesions. Subdural passages were positive (typical encephalitic lesions). The period of incubation lessened in the course of passages (ten, eight and four days). The strain is keratogenous; the keratitis is complicated by fatal neuraxic phenomena. Those rabbits which survive corneal inoculation with encephalitic virus of the Vienna strain resist the herpetic virus; conversely, herpetic keratitis confers corneal immunity to the encephalitic virus. This applies also to the intravenous inoculation of herpes (cerebral immunity to the virus of encephalitis). This strain and the virus of herpes are therefore identical.

(*g*) Hogander strain (Doerr and Zdansky [38]).—The encephalon from a typical case of encephalitis was sent in glycerin by Kling. Corneal inoculation was made into several rabbits. One of them developed a double keratitis after forty-eight hours. Eleven days later, there appeared "mouvements de manège"; the animal succumbed on the twentieth day. Typical lesions were found, intradural passages were positive. The strain is keratogenous. Cross-immunity experiments (herpes-encephalitis) show that this strain is identical with the virus of herpes.

(*h*) In addition to these strains, there is the virus isolated in France by Netter, Césari and Durand [39] from cases of typical encephalitis. Unfortunately, it has been only incompletely studied,

36. Schnabel: Wien. klin. Wchnschr. **36**:84, 1923; Klin. Wchnschr. **1**:1685, 1922.

37. Luger and Lauda: Ztschr. f. ges. exper. Med. **39**:1, 1924.

38. Doerr and Zdansky (footnote 28, first reference); Ztschr. f. Hyg. u. Infectionskrankh. **102**:1, 1924.

39. Netter, Césari and Durand: Compt. rend. Soc. de biol. **84**:854, 1921.

although the symptomatology of the experimental disease resembles that of the infection caused by the aforementioned strains (nervous disorders and typical lesions; salivation).

There is further to be considered a strain isolated at Vienna by Paltauf and Koritschoner.[40] This strain was studied in great detail by Luger and Lauda [37] and by Doerr and Zdansky.[41] The former considered it herpetico-encephalitic in nature, but with somewhat peculiar characteristics. When inoculated cerebrally, the virus causes paralytic disorders (epidemic type) after from three to five days' incubation. It is virulent for the mouse, the guinea-pig, the rabbit, and, as Paltauf and Koritschoner observed, the dog. Inoculated corneally, this strain does not produce keratitis, but causes the paralytic disorder (we have confirmed these observations).

Doerr and Zdansky reported the clinical history of the patient from whom the Koritschoner strain was derived. The subject, six weeks after being bitten by a dog believed to be rabid (no histologic or experimental test for canine rabies), and after undergoing antirabic treatment, was admitted to a hospital, where he died with clinical and microscopic symptoms of encephalomyelitis. The encephalon produced the paralytic disorder in the rabbit, and the passage virus, inoculated into the brain of a dog, after four days' incubation, produced a paralytic infection differing from canine rabies. The lesions in these animals were those of an acute myelo-encephalitis without Negri bodies.

We have also studied this strain, which was kindly sent us by Silberstein. Our experiments confirmed those of Doerr and Zdansky; they showed that there is no connection between the virus isolated by Paltauf and Koritschoner and the herpetico-encephalitic virus of Levaditi and Harvier. Rabbits vaccinated against herpes and encephalitis contract the paralytic disease when inoculated cerebrally with the strain in question. This strain is virulent for the dog, which, on the other hand, is completely immune to the virus of herpes (Blanc) and to the encephalitic virus (our own researches and those of Doerr and Zdansky). The virus is not keratogenous. Further, notwithstanding the absence of Negri bodies, the microscopic lesions resemble those of rabies, so that in view of all these considerations I think it reasonable to regard the virus of Paltauf and Koritschoner as related to the virus of rabies and distinct from the herpetico-encephalitic virus (Doerr and Zdansky).

Several strains of virus isolated from the neuraxes of encephalitic patients have since been studied at the time of the Japanese epidemic of encephalitis in 1924. I may quote among these authors

40. Koritschoner: Wien. klin. Wchnschr. **36**:385, 1923.
41. Doerr and Zdansky (footnote 38, second reference).

Kobayashi,[42] Takagi [43] and Nishibe.[44] The results on record have this in common—they agree neither with each other nor with the results which have been recorded in Europe. Furthermore, from two cases of acute encephalitis Kobayashi isolated a virus (in the brain and spinal fluid) which, injected into rabbits, cats, guinea-pigs and mice, produces this disease after an incubation period of from four to twelve days. The following symptoms were observed; torpor, myoclonus, athetoid movements and paralysis. The author sees a resemblance between the virus he has isolated and that of rabies. In the central nervous system he found forms analogous to Negri bodies; but he also found that the antiserum prepared from the encephalitic virus neutralized in vitro the virus of rabies, and vice versa. Takagi succeeded six times in isolating a virus that was pathogenic for rabbits and which produced torpor, loss of weight, paralysis and myosis. The virus is filtrable, resistant at 0 C. and killed at about 55 C. It is found in the brain, spinal fluid, liver, spleen and salivary glands of infected animals. Takagi found that this virus differs from that of herpes (absence of crossed immunity, Koritschoner's strain).

Nishibe undertook the microscopic study of the experimental lesions recorded in animals infected by the Japanese encephalitic virus. He recognized the fact that this virus is pathogenic for rabbits, polioencephalotrope, filtrable, and transmissible from one animal to another. The lesions are characterized especially by a vacuolar degeneration of the ganglion cells, by definite indications of neuronophagia and by hemorrhage. The author emphasized the absence of vascular and meningeal deterioration.

Since it has been impossible for us to experiment with the Japanese strain of encephalitic virus, I cannot express any definite opinion on the relation existing between the observations outlined and those made in Europe.

COMMENT

The strains described are those of herpetico-encephalitic virus isolated from the neuraxis or cerebrospinal fluid of patients with von Economo's disease.[45] All the researches undertaken with these viruses have confirmed fully the results of the experiments made by Harvier, Nicolau and myself. The principal facts established are:

1. Nothing is more difficult than to transmit encephalitis from man to the rabbit. Harvier and I have obtained only three positive results,

42. Kobayashi: Japan M. World **5**:145, 1925.

43. Takagi: Japan M. World **5**:147, 1925.

44. Nishibe: Repr. from the Scientific Reports from the Government Institute for Infectious Diseases, 1925, vol. 4, p. 223.

45. I shall not dwell here on the viruses studied by Bessemans and von Boeckel (Arch. méd. belges, 1922, no. 4). The experimental results reported by these authors are too inconsistent to merit consideration.

although we have carried out thirty inoculations of the substance of nerve centers, cerebrospinal fluid, nasal mucous membrane, saliva, etc., on rabbits, guinea-pigs and monkeys of inferior orders. Apart from Szymanowski and Zilberblast-Zand,[46] who appear to have registered positive results in 33 per cent of their cases, the majority of the authors who have studied the question (Doerr and Schnabel, Berger, Schnabel, Flexner) have confirmed the difficulty of transmission to animals. Thus Doerr and Zdansky, in a series of recent investigations, achieved only one successful transmission in forty-four inoculations made on the rabbit with the most varied human material.

Flexner[47] and Amoss, who have been systematically studying von Economo's disease since 1919, have made an immense number of experiments, both on the monkey and on the rabbit, but have been no more fortunate; all their efforts have proved vain.

2. When, using the neuraxis or the cerebrospinal fluid, we inoculated several rabbits through the dura mater, only one of these animals contracted encephalitis, while the others remained immune for an indefinite period (Levaditi and Harvier[48]). When killed long afterward, they were found to be free from lesions. What is more, if their sensitivity is tested by ocular or cerebral inoculation of the virus which has proved to be pathogenic for one member of the batch, it is found to be almost indistinguishable from that of rabbits not inoculated previously. It follows that these animals resist the first inoculation for reasons other than natural immunity. What are these reasons?

The facts cited seem to show that in encephalitic subjects the quantity of virus present in the neuraxis is so small that in most cases it is difficult to detect the virus on inoculation into the rabbit. The distribution of the virus in the different segments of the encephalon appears to be subject to variations which, unfortunately, cannot be predicted. Certain centers are richer in organisms, while others are free from them; and it is difficult to know which are the more virulent when one wishes to select them, because in practice one can inoculate into the rabbit only specimens of cerebral material taken at random. Moreover, the actual characteristics of the neuraxic lesions in man show that encephalitic subjects succumb when the infection has become chronic (Levaditi and his collaborators). It is therefore highly probable that at this relatively late stage the encephalon is more or less clear of organisms (autosterilizable neuro-infection). These are a few of the reasons which explain the facts previously stated.

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46. Szymanowski and Zilberlast-Zand: Brain **46**:49, 1923.

47. Flexner, S.: Epidemic Encephalitis and Allied Conditions, J. A. M. A. **81**:1688 (Nov. 17) 1923.

48. The fact has been confirmed by Doerr and his collaborators, and by Schnabel and others.

3. As has been established by my collaborators and me, all the strains isolated are keratogenous, the keratitis being followed by a progression of the disease toward the neuraxis. They are virulent for the guinea-pig and the mouse (Levaditi, Harvier and Nicolau) and nonpathogenic for the dog (Doerr and ourselves).

4. Cross-immunity shows the identity in nature of these strains and the herpetic virus.

What conclusion can one draw from the combination of all these observations except that whenever it has been possible to produce in animals an encephalitic disorder of definitely human origin this disorder was produced by a filtrable and invisible virus belonging to the herpetico-encephalitogenous group? In other words, the view that the virus of herpes plays the chief part in the etiology of von Economo's disease is entirely confirmed.

Unfortunately, this view, though supported by such precise observations, is not unanimously accepted. Numerous objections have been raised, of which the most important is:

The presence of the herpetic virus in the neuraxis of encephalitic subjects is not an absolute proof that it plays an etiologic part in von Economo's disease. This virus might be merely a common organism associated with the still unknown virus of encephalitis. In fact, instances of microbic association between filtrable viruses and cultivable bacteria are abundant in pathology. One need mention only swine fever and exanthematic typhus. Rouillard [49] was the first to point out that in the patient Hoff, from whom the herpetic encephalitic strain isolated by Harvier and myself was derived, clinical examination revealed a facial herpes which was still present at autopsy. It is therefore to be supposed that the virus isolated by inoculation into the rabbit was in this particular case the virus of herpes, which must have invaded the nerve centers through encephalitic lesions in the strict sense of the term. A true symbiosis must have been established between this herpetic virus and the unknown virus of encephalitis. It has been known since the experimental researches of Nicolau and myself [50] that two dissimilar ultraviruses, such as neurovaccine and the virus of herpes, can be associated and live conjointly in the encephalon.

Certain writers, notably Kling and his collaborators, and also Bastai,[19] have not hesitated to take up this observation and turn it against our conclusions. Were they right in doing so? I think not, for the following reasons:

1. The Hoff case is the only one in which an eruption of herpes has been reported in a subject whose encephalon or cerebrospinal fluid

49. Rouillard: Presse méd. **29**:865, 1921.

50. Nicolau, S., and Levaditi, C.: Ann. de l'inst. Pasteur **37**:1, 1923.

has proved virulent for the rabbit. Notwithstanding the virulence of the neuraxis or cerebrospinal fluid of the patients examined by Doerr, Schnabel, Berger, Luger and Lauda and others, none of these patients had visible herpetic eruptions. It follows from this that the existence of the herpetico-encephalitic virus in the nervous system of subjects suffering from encephalitis in no way implies association with a concomitant vesicular exanthem.

2. If the virus of herpes was really an associated organism, it should *a fortiori* be discovered in the neuraxic centers or at least in the cerebrospinal fluid of nonencephalitic herpetic subjects. What does experience tell on this point?

The oft-mentioned researches of Ravaut and Rabeau,[51] which were partly carried out in our laboratory, are well known. The authors, being convinced of the frequent localization of herpes in the nerve centers, as indicated by examination of the cerebrospinal fluid (manifest lymphocytosis, Ravaut and Darré [18]), inoculated rabbits with the deposit from centrifugation of fluid taken from subjects presenting herpetic symptoms at the time. In one of the rabbits which, after receiving injections in the cornea, died on the forty-third day without having developed keratitis, Ravaut and Rabeau observed inflammatory encephalitic lesions without characteristic features and in no way resembling the lesions of experimental herpes. Further, the culture of the brain of this rabbit was positive, which is not the case when infection is produced by the herpetico-encephalitic virus; no passage, however, was carried out. All these facts make the results obtained by Ravaut and Darré questionable.

The same does not appear to be true of the researches recently reported by Bastai and Busacca [52] and by Veratti and Sala.[53]

Bastai and Busacca took cerebrospinal fluid from patients suffering from relapsing herpes labialis of herpetic keratitis and inoculated it intradurally into rabbits. The animals succumbed in ten days. In the opinion of Bastai and Busacca, the virus which was the cause of death was undoubtedly that of herpes; it is keratogenous, and can be maintained by successive passages. Moreover, this virus, when inoculated into man either intracutaneously or through the cornea, engenders specific local lesions (epidermatic vesicles or keratitis) and penetrates the spinal canal. A surprising feature is that it vegetates there for a long time, even after the ectodermic lesions have been cured (months); in the opinion of the Italian authors, this proves the possibility of a latent herpetic infection of the neuraxis.

51. Ravaut and Rabeau: Compt. rend. Soc. de biol. **85**:1132, 1921.
52. Bastai, P., and Busacca, A.: Klin. Wchnschr. **3**:147, 1924.
53. Veratti and Sala: Boll. d. Soc. med.-chir. di Pavia, 1923, vol. 36.

The importance of these experimental data is obvious. Unfortunately, they have yet to be confirmed. None of the authors who have successfully studied the problem have succeeded in verifying the results obtained by Bastai and Busacca. Thus, Schnabel [54] inoculated into the rabbit by the corneal route the cerebrospinal fluid of four herpetic subjects (herpes genitalis), and recorded only negative, or at best doubtful, results. The contents of the herpetic vesicles of the same subjects, however, produced in the animal a typical keratitis. Doerr and Zdansky [41] administered to their rabbits, either by the corneal or by the subdural route, not only cerebrospinal fluid, but also the substance of nerve centers from cases of herpes labialis associated with certain infectious processes (pneumonia). The results were negative. In numerous attempts we ourselves made in collaboration with Nicolau and Poincloux, we never succeeded in producing in the rabbit encephalitis or keratitis by injecting into the encephalon or the scarified cornea cerebrospinal fluid from herpetic subjects (recurrent herpes, Cuid. case [55]).

The results of Veratti and Sala [58] are even less evidential. The authors took cerebrospinal fluid from four subjects suffering from pneumonia accompanied by herpes and inoculated it subdurally in a dose of 0.5 cc. The rabbits succumbed on the twelfth, thirteenth and twentieth days, with nervous symptoms (positive passages). In the brains of these animals, however, Veratti and Sala found none of the characteristic alterations of cerebral herpes, and they said nothing of the keratogenous qualities of their strains. Their conclusions are extremely cautious.

There is thus at present nothing to prove that the herpetic virus is present as frequently as the Italian authors suppose in the neuraxis or cerebrospinal fluid of subjects suffering from herpes simplex or herpetic eruptions associated with infectious processes of any kind, except epidemic encephalitis. The same is true of the existence of this virus in the blood (Bastai, Veratti and Sala) and fecal matter (Veratti and Sala).

Can it be detected in the encephalons of subjects succumbing to infections other than herpes or encephalitis? Numerous researches have been undertaken in this direction, but all have yielded negative results (malaria tropica, endocarditis, pulmonary influenza: Doerr and Zdansky, Doerr and Schnabel). There has been the same lack of success with cerebrospinal fluid (Schnabel, Doerr, ourselves, Flexner).

In three cases, however, Jahnel and Illert [56] stated that they found in rabbits inoculated (by the subcutaneous, scrotal and intratesticular

54. Schnabel, A.: Klin. Wchnschr. **2**:429, 1923.

55. Nicolau, S., and Poincloux: Compt. rend. Soc. de biol. **87**:451, 1922; Ann. de l'inst. Pasteur **38**:977, 1924.

56. Jahnel and Illert: Klin. Wchnschr. **2**:640, 1923.

routes) with cerebrospinal fluid from cases of uremic arteriosclerosis, Wilson's disease, or senile dementia a chronic infection transmissible in series and characterized by spinal lymphocytosis and encephalitic lesions. On reading the reports of these authors, one sees at once that here one is dealing with the epizootic disease of the rabbit (this is amply proved by the nature of the cerebral lesion and the symptoms).

Far be it from me to deny that the herpetico-encephalitic virus is capable of vegetating in the latent state (without engendering encephalitis) in the neuraxis of certain subjects suffering from herpes or even having no cutaneous symptoms. My theory of germ carriers and of the "formes frustes" of von Economo's disease implies such a possibility. I merely argue that in the present state of knowledge there seems to be no unquestionable evidence of it apart from an observation made by Flexner,[47] which is so important that it merits close attention.

Flexner and Amoss had occasion to make a lumbar puncture on a subject, aged 51, who was under treatment for neurosyphilis at the Presbyterian Hospital. This patient also had aortostenosis. The spirochetal infection was of sixteen years' duration. There had never been any question of encephalitis in this case (Flexner did not state whether the patient was subject to herpes). The patient had been treated with arsphenamine and mercury. The cerebrospinal fluid was inoculated into two rabbits subdurally. One remained immune (as in the first of our experiments), while the other was seized with characteristic nervous disorders on the ninth day and succumbed on the fourteenth day (with fever, but without salivation). The virus was found to be definitely keratogenous, and was maintained by successive passages; it was pathogenic by the cutaneous (production of herpetic vesicles), hematic and testicular routes. A second spinal puncture carried out about a month later yielded a less virulent fluid than the first.

This observation shows that in some cases the herpetic virus may vegetate in the cerebrospinal fluid of certain subjects free from encephalitis and apparently in good health. Such results, if confirmed, would support the conception of germ carriers with localization of the virus not only in the saliva and the nasopharynx, but in the neuraxis and cerebrospinal fluid.

In short, none of the objections advanced against the theory that herpes and von Economo's disease have the same etiologic agent, the "herpetico-encephalitic virus," can withstand objective criticism. At the same time, there are still numerous problems to be solved, especially the following:

PREDISPOSITION AND VIRULENCE: EXPERIMENTS ON MONKEYS

Predisposition and Virulence.—Why is it that the herpetic virus, though widespread in man, so rarely produces encephalitis, even in

epidemic periods? Herpes simplex, recurrent herpes and herpes as a complication of infectious diseases are of frequent occurrence, whereas von Economo's disease is seldom encountered. There are at least two factors to be considered: the specific affinities of the virus and the medium.

Man enjoys a certain degree of natural immunity to the encephalitic virus; in most cases, this immunity is sufficient to prevent the penetration of the virus into the neuraxis and the development of the disease. For many reasons this natural refractory state is impaired in certain subjects; in them alone the virus which they carry in their systems, or acquire by contact with encephalitic subjects, succeeds in multiplying and engendering the infection (Levaditi and Harvier, 1920). Experiments on *Catarrhina* monkeys and anthropoid apes support this theory of the etiology of epidemic encephalitis (Levaditi and Nicolau[57]).

In the first place, it has been established that of the inferior simians (*Macacus cynomolgus, Macacus rhesus, Cercocebus fuliginosus, Cynocephalus hamadryas*) and anthropoids (chimpanzees) inoculated by the cerebral route with our encephalitic virus, strain C., only a few of the inferior *Catarrhina* monkeys have contracted encephalitis. I give here the clinical and anatomopathologic history of these receptive monkeys:

1. On April 16, 1924, *Cercocebi* 18 and 19 were inoculated intracranially. Monkey 19 proved to be refractory, but monkey 18 was seized with trembling and paresis on the sixth day. On the following day, it was found lying down, suffering from a generalized paralysis accompanied by somnolence. On the eighth day, the paralysis was complete; respiration was scarcely perceptible; convulsions and myoclonia were present. The animal died on the ninth day.

Histologic Examination.—The lesions were marked, particularly on the anterolateral cerebral cortex, the central nuclei, the mesencephalon and the pedunculi. Perivascular cuffs were observed, constituted of lymphocytes and especially of polymorphonuclears. Cortical and subcortical foci of acute encephalitis, with polymorphonuclear elements, were numerous; in the adjacent area we found an extremely marked neuronophagia, with profound lesions of the nerve cells resembling the lesions found in the "elective zone" in the rabbit. No alteration was detected in the hippocampus, the cerebellum or Ammon's horn, whereas the pons varolii, the medulla oblongata and certain segments of the marrow showed definite lesions (cuffs and foci of parenchymatous inflammation).

Fragments of encephalon taken from this monkey were inoculated by the cerebral route into two rabbits (767 and 768). These animals died of encephalitis, one on the fourth day and the other on the fifth (microscopic examination).

Comment.—This experiment shows that intracerebral inoculation of encephalitic virus C, having undergone a large number of passages through the rabbit (from 1920 to 1924), produced a fatal encephalitis in a *Cercocebus fuliginosus*, virulent viruses being present in the enceph-

57. Levaditi, C., and Nicolau, S.: Compt. rend. Soc. de biol. **90**:1372, 1924.

alon. This encephalitis was of a superacute character, as witness the peculiarities of the lesions of the neuraxis.

2. On March 8, 1920, we inoculated the same strain C, just isolated from man (it had undergone only four passages through the rabbit), into *Cynomolgus* 54 (intracranial inoculation, Levaditi and Harvier's experiment[58]). The animal appeared to be ill on the eighth day, showed signs of nystagmus and moved with difficulty. The disease proved worse on the following day; somnolence developed, and death took place on the twelfth day.

Histologic Examination.—Encephalomedullary alterations were similar to those in the previous monkey, with the difference that in this case the elements of the lymphocyte series greatly predominated. The perivascular cuffs and the encephalitic foci were largely formed by lymphocytes, plasma cells and large mononuclears.

Fragments of the brain of this monkey were inoculated by the cranial route into two rabbits (24 and 25). Both died of encephalitis (fourth and fifth days).

Comment.—This second experiment shows that a *Macacus cynomolgus*, inoculated with encephalitic virus C, contracted a fatal encephalitis, virulent viruses being present in the neuraxis. Histologically, this encephalitis presented pronounced characteristics, and in all respects resembled von Economo's disease.

3. On Nov. 30, 1923, three monkeys of the species *Macacus cynomolgus* were inoculated cerebrally with the same strain C. Only one (monkey 43) contracted the disease. On the tenth day, the animal moved with difficulty and reacted to every stimulus by clonic convulsions. On the following day, it presented paresis and bilateral epileptiform crises, myoclonic spasms, nystagmiform movements, head thrown backward and panting respiration. Coma and death ensued.

Histologic Examination.—Meningitis of the cortex and septums, featured by lymphocytes and large mononuclears, was present. Perivascular cuffs with lymphocytic elements were present. Foci of acute encephalitis were found in the medulla oblongata and pons varolii. These lesions were also found in the mesencephalon and the marrow.

Fragments of encephalon were inoculated by the cerebral route into two rabbits (17 B and 18 B), which survived; they proved receptive at a subsequent test (nineteen days later).

Comment.—This third experiment shows that a *Macacus cynomolgus*, inoculated with our encephalitic strain C, contracted a fatal encephalitis, but that no virulent viruses could be detected in the encephalon by inoculation into the rabbit.

4. Two chimpanzees were inoculated intracranially with the same virus on Dec. 5 and 22, 1923; they resisted absolutely.

These facts prove that the monkey is, as a rule, refractory to the encephalitic virus isolated from man and maintained by passages through the rabbit, even when the virus is introduced direct into the encephalon. Certain monkeys, however, are exceptions to this rule. As a consequence of the impairment of their natural resistance, they contract encephalitis,

58. Levaditi and Harvier (footnote 1, second reference).

which may differ in type in different cases; the condition may be acute or chronic encephalitis, both virulent for the rabbit, or fatal meningo-encephalitis without viruses in the encephalon.

Between these experimental data and the observations made on man there is a striking analogy. The simian and human species are not capable of contracting encephalitis unless, for special reasons (hereditary or acquired), the natural refractory state proper to these species is impaired. This sufficiently explains the contrast between the frequency of herpes and the rarity of encephalitis. The virus of herpes, being ubiquitous, easily localizes itself on the skin, the mucous membranes and the cornea, because these segments of the ectoderm in this regard offer a receptivity appreciably greater than that of the neuraxis, an invaginated portion of the same ectoderm. It will not attack the nervous system unless the natural immunity of that system is diminished. Changes in the medium and augmentation of the neurotropic affinity of the virus are the essential determining factors of von Economo's disease.[59]

Thus the intracerebral inoculation of herpetico-encephalitic virus C produces in the inferior simians (*Macacus cynomolgus*) a type of encephalitis identical in evolution and microscopic lesions with epidemic encephalitis in man. Acute or chronic forms, the presence of virus in the neuraxis at the time of the animal's death or total sterility of the encephalon (fatal autosterilizable neuro-infections of Levaditi, Sanchis-Bayarri and Schoen[60]) all represented analogies between the experimental disease and encephalitis in man. On the other hand, the neuraxic alterations (monocytic perivascular cuffs, inflammatory microgliar foci, degeneration of the nerve cells and neuronophagia) were dispersed. Affecting the whole system of encephalon, mesencephalon, pedunculi and even the medulla, these alterations did not present that special mesencephalic localization met with in most cases of von Economo's disease. Since then,[61] however, we have had occasion to observe a monkey suffering from experimental encephalitis characterized by this almost exclusively mesencephalic topography of the microscopic lesions. The details of our observations are here given.

Macacus sinicus 6.—On June 23, 1927, intracerebral inoculation was made of 1 cc. of emulsion prepared from the brain of rabbit 903 Z, which died of herpetic encephalitis four days after transcranial inoculation with the passage virus of

59. The history of the monkey that was the subject of our third observation is particularly interesting. It shows that an animal may succumb to encephalitis although no virulent viruses may be detected in its brain by inoculation into the rabbit. Similar cases have frequently been observed in man; we have found that inoculation of material from the brains of encephalitic subjects into the rabbit seldom yields positive results.

60. Levaditi, C., Sanchis-Bayarri, and Schoen, R.: Compt. rend. Soc. de biol **98**:911, 1928.

61. Levaditi, C., and Schoen, R.: Compt. rend. Soc. de biol. **98**:1189, 1928.

herpes (strain N). On July 2, nine days after inoculation, the monkey showed signs of collapse and underwent epileptiform crises with stiffening of the back of the neck; in the intervals between these crises it recovered, but again relapsed into the same convulsions. On the following days, there were pareses (at first localized and afterward generalized), somnolence and coma. The animal died on the eleventh day. At the postmortem examination we found hyperemia of the basal meninges, congestion of the liver and occasional whitish spots on the surface of the spleen. Cardiac and cerebral blood cultures were negative. An emulsion was prepared with fragments of encephalon and was inoculated by the intracerebral route into rabbits 12 and 13 A; on the sixth day, these animals succumbed to herpetic encephalitis which was confirmed histologically and by subsequent passages.

Histologic Examination of the Neuraxis.—The alterations were localized in the central nuclei and the mesencephalon. Microscopic examination of the frontal, parietal and occipital cortex, the cerebellum, the hippocampus major, the cervical, dorsal and lumbar marrow and the spinal ganglia revealed no cellular, parenchymatous or vascular lesions. This was not the case in the central nuclei and the mesencephalon.

In the central nuclei there were profound lesions. Foci of acute encephalitis were present, principally around the vessels. There was oxyphilia of the white matter in the vicinity of these foci which were composed of monocytes (lymphocytes and plasma cells) and especially of karyolysed polymorphonuclears. There were marked alterations of the nerve cells: achromatosis, chromatolysis, vacuolization in the cytoplasm, vesicular nuclei with increase of oxychromatin and accumulation of basichromatin toward the nuclear membrane. Signs of neuronophagia were found here and there. The vessels were surrounded by cuffs consisting of lymphocytes and plasma cells.

In the mesencephalon, especially in the cerebral peduncles (locus niger), foci of acute encephalitis were present, particularly near the quadrigeminal tubercles and the locus niger. There was slight monocytic meningitis. Alterations were present in the nerve cells, though they were less marked than those around the central nuclei. Frequent and well developed perivascular cuffs were present.

The bulbar lesions consisted of small foci of neuronophagia, somewhat dispersed; most of the neurons of the bulbar nuclei presented a normal appearance.

Comment.—It will be seen that the intracerebral inoculation of the passage virus of herpes (strain N) into a *Macacus sinicus* produced acute encephalitis, developing in two days and terminating in the death of the animal; the encephalon contained herpetic viruses virulent for the rabbit. This observation is particularly interesting because the localization and the microscopic characteristics of the encephalitic alterations are identical with those habitually encountered in epidemic encephalitis in man. Thus intracerebral inoculation either of the herpetico-encephalitic strain C, isolated by Harvier and myself from the encephalon in a case of von Economo's disease, or of the herpetic virus proper (herpes labialis), in certain inferior simians produces the various types of epidemic encephalitis found in man, the identity being shown not only by the characteristics and evolution of the disease, the virulence or sterility of the neuraxis and the peculiarities of the microscopic lesions, but by the topography of the lesions.

VARIATIONS IN THE NEUROTROPIC, CORNEOTROPIC AND DERMATOTROPIC AFFINITIES

There is now to be considered the influence of the intrinsic virulence of the virus on the variations in its neurotropic, corneotropic and dermatropic affinities. This question was studied by us in 1922;[62] we supplemented these facts by further observations reported in a paper presented before the Société de Biologie[63] in collaboration with Nicolau and Poincloux. Its substance is as follows:

We examined the following strains: (*a*) the herpetic virus, Blanc strain,[64] maintained by frequent passages through the rabbit; (*b*) our encephalitic strain C, the origin and characteristics of which have been described elsewhere;[58] (*c*) a new herpetic strain, Am, isolated from a woman suffering from recurrent herpes. These three strains were studied with reference to their corneotropic and dermatotropic affinities.

1. *Corneotropic Affinity.*—The experiments were made on the chimpanzee.

(*a*) A female chimpanzee was inoculated by scarification of the left cornea (Dec. 7, 1923) with a thick emulsion of encephalitic virus C. There was no reaction. The same cornea was inoculated a second time on Dec. 22, 1923, with the same negative result. On a third occasion we again inoculated the right cornea of this chimpanzee, still without success.

(*b*) A male chimpanzee was scarified on the left cornea on Dec. 24, 1923, with herpetic virus Am. Keratoconjunctivitis appeared on the fourth day, lasted six days, and then was completely cured.

Was this keratitis herpetic? Experience dictates an affirmative answer. On the fourth day of its development, we took material from the cornea and the conjunctiva and inoculated it by the corneal route into rabbits 252 and 253 and by the cutaneous route into rabbit 250. The first two animals developed keratitis and succumbed to encephalitis on the tenth day, while rabbit 250 presented a herpetic eruption on the skin.

This experiment brings out the distinct difference between the corneotropic affinity of the encephalitis virus C and the corresponding affinity of the herpetic virus Am, as estimated on the basis of the results yielded by inoculation into the chimpanzee. Whereas the first named virus proved incapable of producing keratitis, the herpetic virus in the same conditions caused an intense keratoconjunctivitis transmissible to the rabbit. It follows that in accordance with our conception the virus of epidemic encephalitis, though it belongs to the same group as the herpetic virus, differs from the latter not merely in its neurotropic affinity, which is generally more marked, but in that it is less capable of pullulating on the corneal segment of the ectoderm (chimpanzee).

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62. Levaditi, C., and Nicolau, S.: Compt rend Soc. de biol. **87**:1102, 1922.
63. Levaditi, C., and Nicolau, S.: Compt. rend. Soc. de biol. **90**:1376, 1924.
64. Blanc and Caminopetros: Compt. rend. Soc. de biol. **84**:629, 1921.

2. *Cutaneous Affinity.*—The degree of this affinity was determined by inoculating the three strains into the skin of the rabbit, after depilation, shaving and scarification (Calmette-Guérin method).

Rabbit 327 was inoculated with the Blanc herpetic strain. On the fourth day, small and slightly vesicular papules appeared, surrounded by squamae and by a pinkish areola. These vesicular papules had a distinctly herpetic appearance. The animal survived. It was killed on the twenty-ninth day. No lesions of the central nervous system were found.

Rabbit 324 was inoculated with Am herpetic strain. On the fourth day, five small papules were observed. These subsequently became vesicular, and were superficially eroded and ulcerated. They were larger than the vesicular papules produced by the Blanc herpetic strain. The animal died paralyzed on the twelfth day. Microscopic examination revealed a slight meningo-encephalitis and profound alterations of the segment of the spinal cord corresponding to the cutaneous surface inoculated. These alterations consisted in a poliomyelitis affecting both the anterior and the posterior horns, with neuronophagia and perivascular cuffs. Lesions were also observed in the vicinity of the spinal ganglia (chromatolysis and neuronophagia).

Rabbit 325 was inoculated with encephalitic strain C. On the fourth day a discrete papulosquamous miliary eruption was observed. This eruption was less intense and more transient than that produced by the two herpetic strains previously studied. The animal died on the twelfth day. Microscopic examination revealed the same alterations as in rabbit 324, but they were slightly less marked.

The characteristics and the evolution of these cutaneous eruptions prove that the dermatotropic affinity of our three strains of virus differs in different viruses. Highly pronounced in the Am herpetic strain, also well marked in the Blanc herpetic strain, this affinity is scarcely perceptible in the encephalitic virus C. According to the results of the experiment on the chimpanzee (cornea), the virus of von Economo's disease seems less capable of producing macroscopic and microscopic lesions of the cutaneous integument than the two strains of herpetic origin.

These researches show that the encephalitic varieties of the virus of herpes possess affinities different from those of the herpetic strains properly so called. Less capable of attacking the ectodermatic segments, the cutaneous integument and the cornea (chimpanzee), they are more acclimatized to the neuraxis, and consequently more virulent for the central nervous system.

If, therefore, certain human subjects seem more predisposed than others to von Economo's disease, the reason is that in them the two determining factors referred to occur simultaneously. First, the medium offers a special receptivity to the virus which these subjects carry in them or acquire by contact with cases of the disease; second, they are infected by strains of herpetico-encephalitic viruses which seem to be intrinsically better adapted to the neuraxis. Changes in the medium and augmentation of the neurotropic affinity of the virus are the essential determining factors of von Economo's disease.

AUTOSTERILIZABLE NEURO-INFECTIONS

There is one problem—a problem of paramount importance and, indeed, of a most disturbing nature—which needs elucidation. It has reference to the sterility of the neuraxis—as judged from the results of inoculations into laboratory animals—which is so frequently found in encephalitic subjects. How is it that in spite of innumerable attempts at transmission, viruses belonging to the herpetico-encephalitic group of ultraviruses have been isolated in so few cases? We have endeavored to solve this problem by means of experiments performed with encephalitis, herpes and rabies viruses, and have thus built up the theory of "autosterilizable neuro-infections,"[60] which, in general outline, is as follows:

When the neurotropic ultraviruses develop in contact with the constituent elements of the neuraxis, the latter reacts by lesions affecing the neurons, the neuroglia, the microglia and also the vasculoconjunctive system, with which the last named is intimately connected. These lesions have a twofold significance: 1. They reflect the nucleocytoplasmic degeneration produced by the pullulation of the virus in contact with the constituent elements of the neuron. 2. They reveal a defensive process similar to any inflammation of microbial origin. To the first category should be ascribed the alterations of the neuron in rabies, epidemic encephalitis, poliomyelitis and herpes—chromatolysis, achromatosis, vacuolization, nuclear oxyphilia (Lipschütz' body). These alterations frequently result in the total disintegration of the infected cell. To the second category should be ascribed pericellular diapedesis, neuronophagia, the mobilization of and the morphologic changes in the microglia (granulo-adipose cells), and the meningeal and perivascular monocytary reactions. The clearly defensive nature of neuronophagia is shown by the fact that the phagocytes, enveloping the remnants of the degenerated nerve cells, ingest the virus which has been developing in these cells (poliomyelitis Levaditi and Pignot[65]). In this case, therefore, we are concerned with a process directed toward the destruction of the virus in situ, an indispensable condition for the cure of the neurotropic infection. If such a process took place in a tissue other than the neuraxis, a favorable result would be quickly attained. But the position is different when these defensive reactions occur in tissue as indispensable to life as the neuraxis. Usually, the animal dies of severe nervous disorders, for the reason that the intensity of the reactions mentioned becomes incompatible with the normal functioning of certain encephalomedullary centers. Degenerative and inflammatory alterations and the presence of the virus in more or less considerable quantities are the most commonly observed characteristic features of neurotropic infections.

65. Levaditi and Pignot: Ann. de l'inst. Pasteur **28**:509, 1914.

There are, however, exceptions to which I should like to draw attention. During the course of our research work on the herpetico-encephalitic virus, we found that certain rabbits which had been inoculated by the intracerebral route died belatedly from intercurrent infections, after showing symptoms of nervous disturbances which were usually transient. The histologic examination of the encephalon sometimes showed the presence of intense, yet circumscribed, alterations, which we termed "chronic lesions" to distinguish them from the marked alterations found in animals that died within the usual time. They consisted of cortical or subcortical foci from which the neurons had almost entirely disappeared, being replaced by a microglial tissue containing a high proportion of granulo-adipose cells. The inoculation of material from such encephalons into fresh rabbits generally gave a negative result, thus demonstrating the sterilization of the neuraxis.

Therefore, the defensive process must have succeeded in destroying the germs which had pullulated in contact with the neurons and in clearing out the disintegration products of the lysis of these neurons, subsequently taking a cicatricial form consistent with the survival of the animals for varying lengths of time. Another example is afforded by certain monkeys which when inoculated with poliomyelitis virus survive with residual paralyses due to persistent though entirely virus-free medullary alterations (Landsteiner-Levaditi [66]). However, it may also happen that animals die of nervous disorders and with intense neuraxic lesions in cases in which the defensive process had succeeded in destroying the virulence of the virus. In a recent paper,[67] we reported cases of this kind, including that of a rabbit which was infected with encephalitis virus C (intracerebral and corneal route) and which died on the fourteenth day with acute encephalitic lesions, but without any virus in its encephalon.

Following is another instance: Encephalitis virus C was inoculated intracerebrally into rabbit 398. The animal died on the twenty-fifth day, the symptoms observed being salivation and difficulty in maintaining balance. The brain showed encephalitic alterations, but the inoculation of material from this brain into rabbits 559 and 560 did not cause any effect. It will be remembered, moreover, that as early as 1924, Nicolau and I [57] showed that the lower *Catarrhina* (genus *Macacus cynomolgus* in the case in point) when inoculated with encephalitic virus C could contract fatal encephalomyelitis without any viruses virulent for the rabbit being found in the neuraxis, in spite of the presence of acute encephalitic alterations. More recently, Gildemeister and Herzberg [68]

66. Landsteiner, and Levaditi, C.: Ann. de l'inst. Pasteur **24**:883, 1910.

67. Levaditi, C.; Sanchis-Bayarri, V., and Reinie: Ann. de l'inst. Pasteur **41**:1292, 1927.

68. Gildemeister and Herzberg: Klin. Wchnschr. **6**:603, 1927.

recorded similar observations. According to these authors, there is no connection between the intensity of the neuraxic alterations and the herpetic virus content of the nervous system, as the herpes virus can determine the outbreak of fatal encephalitis without any trace of it being found in the rabbit's brain.

Hence this fact is established beyond doubt so far as herpes and encephalitis are concerned. What makes it more striking and lends it a certain general significance is that it can occur during the course of rabic infection. Thus, certain rabbits that received several intraspinal injections of ether-treated rabies virus (Marie and Mutermilch method [69]) and were subsequently tested died of rabies, with rabic cerebral alterations but without the virus being present in the neuraxis. The following is an instance:

> Rabbits 645 and 647 N. were given intraspinal injections of fixed ether virus. There was no apparent reaction. They were tested by intracerebral inoculation of fixed virus four days after the last vaccinating injection. The animals died of rabies, one on the eighth day and the other on the sixteenth. There were intense rabic lesions. Passages of fresh brain substance and glycerinated encephalon yielded negative results (complete sterilization).

These examples are sufficient to justify our previously stated conclusions.[67] "It is possible that during an infection with neurotropic virus death may occur at a moment when the inflammatory reactions of the encephalon (reactions of a definitely defensive character) have brought about the complete destruction of the inoculated virus. If this should be so, it may be assumed that these defensive reactions succeed at times in sterilizing the neuraxis, and by their localization and intensity cause the death of the animal." We have called these processes "fatal autosterilizable neuro-infections" which might be contrasted with Nicolle's "nonapparent infections." In the latter, the virus pullulates in the brain (exanthematic typhus of guinea-pigs) without giving rise to any violent outburst of symptoms and without causing death, whereas in the former the animal dies at a stage at which the defensive reactions have already succeeded in sterilizing its neuraxis.

This view is calculated to explain the apparently paradoxic circumstance that on most occasions it has proved impossible to detect the virus in patients suffering from acute or chronic epidemic encephalitis by inoculating material from their nerve centers into the rabbit, and that the same results have been obtained in studying the etiology of postvaccinal encephalitis. Indeed, it is possible that in such patients the defensive reactions, by reason of their intensity and localization, have destroyed the virus, at the same time causing death.

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69. Marie, A. C., and Mutermilch, S.: Compt. rend. Acad. d. sc. **184**:911, 1927.

Recently, Lépine [70] made a personal contribution to this question of autosterilizable neuro-infections. He had occasion to study, in our laboratory, the virulence of the neuraxis and the nature of the microscopic lesions in a number of rabbits which had died with nervous disorders a considerable time after inoculation with herpetic or encephalitic virus by the intracerebral route. Lépine found, as we had done before, that this virulence may be nil, which shows that the animals died as a result of the defensive reactions of the nervous system when the said reactions had succeeded in completely destroying the virulence of the virus.

It should be observed that certain rabbits in which this fatal autosterilizable neuro-infection had developed exhibited a partial resistance, either innate or acquired, which seems to be one of the circumstances favoring the development of such autosterilizable neuro-infections. The case of animals partially vaccinated by the spinal route against fixed rabies virus is an example of this. Lépine quoted another instance as follows:

> For five months rabbit 128 received intramuscular injections of encephalitic virus. It was tested first by intracerebral inoculation of virus C, and was resistant. A second inoculation, given 121 days later, killed the animal in sixteen days. It displayed intense generalized lesions of acute encephalitis, accompanied by degeneration and karyolysis of the cells of the outer and middle zones of Ammon's horn. Nevertheless, material from this brain, when inoculated into rabbit 659 B, produced no disorders in that animal, which survived and showed no lesions when killed.

Lépine stated the belief "that it was the previously engendered condition of relative immunity" which enabled rabbit 128 to sterilize such intense and generalized lesions. This is a point which must not be lost sight of when one is dealing not with the herpetico-encephalitic virus, but with so regularly fatal a disease as rabies. The animals which were observed by Sanchis-Bayarri, Schoen and myself to die with autosterilized lesions had been given three intraspinal inoculations of fixed ether virus before the test injection. Unlike Remlinger,[71] we do not believe that a vaccinating intraspinal injection is an aggravating circumstance which militates against the hypothesis of autosterilization. The encephalon of such animals displays the most intense rabic cellular lesions, pointing to an attack of disease of which it is futile to seek the explanation in the action of a rabic toxin. In the example of the inoculation of filtrates of rabic brain, the passages of which may remain negative, quoted by Remlinger, it would seem more correct to adduce as an explanation the dilution of virus which has been rarefied by filtering through the bougie. Even the death of the animal on the eighth day

70. Lépine, P.: Compt. rend. Soc. de biol. **99**:388, 1928.
71. Remlinger, P.: Compt rend. Soc. de biol. **99**:118, 1928

after inoculation in one case is no cause for surprise in a test on a vaccinated animal, since the response to acute infection was intense neuronophagia—"precisely this being the cause of death."

Accordingly, I think it possible to assume that the coming into operation of the autosterilizable neuro-infectious process is the resultant of the concomitant action of two factors, namely, the acquired or innate refractory condition and the comparatively attenuated virulence of the virus. This is proved by the fact that I have never encountered any cases of autosterilizable neuro-infections except with herpetico-encephalitic strains of relatively weak pathogenic activity or with herpetic viruses of low initial virulence.

The negative results of attempts at transmission undertaken with the neuraxes of patients who have died from postvaccinal encephalitis would seem to show that here again one is dealing with an autosterilizable neuro-infection. For up to the present, attempts to discover a specific, vaccinal, encephalitic, herpetic or other virus in the neuraxes or cerebrospinal fluid of patients suffering from postvaccinal encephalitis have, with one exception, led only to negative results.[72] All the attempts at transmission reported by Levaditi, Bijl and Nicolau,[73] Leiner,[74] Frommel and Baumgartner,[75] Kraus and Takaki,[76] Bijl,[77] among others, have been fruitless. In rabbits inoculated by the intracutaneous or intratesticular route, McIntosh and Turnbull[78] alone have obtained lesions which were transient and not characteristic, but the subsequent transference of which on the cutaneous integument caused the appearance of a few scattered vaccinal pustules. Nicolau and I have pointed out elsewhere what view should be taken of the latter experiments. There is nothing surprising in the fact that it is possible to detect a few isolated vaccinal viruses in the encephalon of patients who died a few days after the appearance of the cutaneous pustules. This is a usual occurrence, which reflects the generalization of the infection but scarcely proves the vaccinal nature of encephalitis (as regards this generalization the work of Paschen should be considered).

Recently, we[79] undertook an experimental investigation of a fresh case of postvaccinal encephalitis, the neuraxis of which was supplied to

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72. For the etiology of this form of encephalatis, reference should be made to Levaditi, Nicolau and Sanchis-Bayarri: Presse méd. **35**:161, 1927.

73. In Bastianse, Therburg, Bijl and Levaditi: Bull. Acad. de méd., Paris **93**:29, 1925.

74. Leiner: Med. Klin. **12**:441, 1926.

75. Frommel and Baumgartner: Schweiz. med. Wchnschr. **56**:857, 1926.

76. Kraus and Takaki: Med. Klin. **21**:1872, 1925.

77. Bijl: Versl. en Mededeelingen betr. de Volksgesondheit, 1927, p. 1471.

78. McIntosh and Turnbull: Brit. J. Exper. Path. **7**:181, 1926.

79. Levaditi, C.:; Lépine, P., and Troisier: Bull. Acad. de méd., Paris **100**:818, 1928.

us by Dr. Bijl of Utrecht. Attempts at transmission performed on the chimpanzee, *Macacus rhesus, Cynocephalus hamadryas, Cercopithecus pathas,* the rabbit, the mouse and the chick showed that even when working under the best experimental conditions, and when using an animal species as closely related to man as the chimpanzee, it is impossible to discover jennerian vaccine or any other known or unknown ultravirus in the neuraxis of patients who have died from postvaccinal encephalitis.

The only conclusion that can be drawn from these facts is that in postvaccinal encephalitis, as in certain cases of herpes or of experimental rabies, one is dealing with infectious processes of the neuraxis coming under the heading of fatal autosterilizable neuro-infections. This conclusion is strengthened by the fact that epidemic poliomyelitis affords instances similar to those mentioned. Thus, in a recent publication, Jonesco-Mihaesti [80] gave an account of the observations of experimental poliomyelitis obtained during the epidemic of infantile paralysis which occurred in Roumania in 1927. (The report of Longhin and Auriau to the Office international d'hygiéne publique, session of May, 1928, may also be consulted.) The author found that certain Roumanian poliomyelitic strains are capable of producing fatal poliomyelitis in monkeys, and that the animals die at a stage when their neuraxis has become incapable of producing the disease in other fresh simians. Nevertheless, the spinal cord of such monkeys displays characteristic and intense poliomyelitic alterations. From all these particulars concerning encephalitis, herpes, rabies and postvaccinal encephalopathy, I therefore infer that the frequent avirulence of the neuraxis of patients who have died following an acute attack of von Economo's disease may be due, not only to peculiarities inherent in the etiologic agent of the disease, but to the fact that the defensive reactions of the neuraxis succeed in sterilizing the virus or in rarefying it to a point at which the infection becomes nontransmissible to the most receptive laboratory animals. *Epidemic encephalitis would therefore be essentially an autosterilizable neuro-infection.*

CONCLUSION

I have now reached the end of my statement. To say that the etiologic problem of epidemic encephalitis is now completely solved would be going too far. Appreciable progress has, it is true, been made since the first research work of Harvier and myself, especially after the relationship between the herpes virus and that of von Economo's disease was understood. It led to the unicist theory, the only one, in my opinion,

80. Jonesco-Mihaesti: Compt. rend. Soc. de biol. **99**:12, 1928.

that fits the experimental facts. While the objections to it are easily refuted, it is none the less true that the isolation of more and more encephalitic strains is desirable. The future will afford research workers the opportunity of supplying the deficiency; but the results already obtained are far from negligible. Above all, no surprise should be felt if continuous efforts prove necessary to reach the goal.

There are diseases which call for experiments on a large number of animals possessing a receptivity approaching that of man, such as anthropoid apes and the lower *Catarrhina*. Encephalitis of the von Economo type is a case in point. My co-workers and I shall, therefore, proceed with our research work, which is greatly facilitated by the support of the Matheson Foundation, for whose valuable services no praise can be too great. In the meanwhile, we stand by the conclusions to be drawn from our first work on encephalitis, as there is nothing to induce us to change our opinion. The only thing that could shake our conviction on this point would be the discovery of an etiologic agent entirely different from that of the herpetico-encephalitic virus. Should such a discovery be made, we should be the first to accept its implications.

RELATIONSHIP BETWEEN EPIDEMIC ENCEPHALITIS AND EPIDEMIC POLIOMYELITIS

Epidemic encephalitis and poliomyelitis, as well as rabies, belong to the same group of infectious diseases caused by a filtrable virus possessing an elective affinity for the nervous system. The relationship is closer, however, between the first two diseases than between either of them and rabies. They are transmitted by the same route, the nasopharynx; they are propagated by "formes frustes" and germ carriers; they are characterized by the same localization of the microbe in the central nervous system and by the same virulence of the nasopharyngeal mucous membrane. The similarity between Heine-Medin's disease and that of von Economo is so close that the experimental study of the latter was in a sense a copy of that of poliomyelitis. Nevertheless, fundamental differences between the two diseases warrant the assumption that they are due to specific viruses. These differences are clinical, anatomopathologic and experimental. They are as follows:

Clinical Considerations.—All observers agree in drawing a clear distinction between the symptomatology, the course and the sequelae of these diseases.

Anatomopathologic Considerations.—Poliomyelitis attacks chiefly the spinal marrow, whereas encephalitis usually affects the mesencephalon, sometimes the cerebral cortex, but rarely the spinal marrow. It is true that encephalitic forms of Heine-Medin's disease have been described, just as discrete medullary lesions have been observed in von Economo's

disease (Harvier and Levaditi). But these are merely exceptions; they in no way detract from the elective localization of the two viruses. Moreover, the cellular reactions of the cerebrospinal fluid [81] are different in the two diseases.

Similar differences are found in respect to histologic lesions. In poliomyelitis, both in man and in animals, the process is acute and is marked by serious and profound alterations of the motor and sensory neurons of the spinal cord. They take the form of neuronolysis and neuronophagia, the mechanism of which, according to the hypothesis worked out by one of us jointly with Landsteiner,[66] is as follows:

> The fact that the nerve cells show degenerative alterations at a time when the perivascular infiltration is comparatively slight shows that the virus (or the toxic products which it gives off) acts on the cells from the outset; the degeneration of the neurons does not depend on the vascular lesions. Similarly, the alterations of the blood vessels and of the meninges cannot be ascribed with certainty to the initial disintegration of the nerve cells, for the virus can itself produce such alterations. The microbes of poliomyelitis invade the nervous system by working along the lymphatic spaces which surround the blood vessels. On reaching the gray matter the parasite attacks the nerve cells and penetrates into their protoplasm, where it multiplies. The pullulation of the virus, possibly also the secretion of some toxin, produces first the initial degeneration of the neuron and, second, an inflammatory reaction around the neuron, consisting of polymorphonuclear and mononuclear cells. Under the necrotic action of the microbe (or of its secretions) the leukocytes degenerate in turn, and the final result of this first phase of the process is thus an accumulation of distintegration products subsequently to be reabsorbed. It may be that in breaking down the polymorphonuclear cells release a proteolytic ferment which, acting on these disintegration products, dissolves them in part. However this may be, it is the Metchnikoff macrophage or Wickmann polyblast mononuclear cells which, by phagocytosis, ensure the final reabsorption of the remains of the nerve cell. The polymorphonuclear reaction is an infection reaction which is bound up with the invasion of the neuron by the virus, whereas the reabsorption of the products of necrobiosis is effected by the macrophages.

In encephalitis in man it is the meningeal and vascular alterations that predominate to such an extent that the perivascular cuffs, consisting of lymphocytes, large mononuclear cells and plasma cells, can be regarded as characteristic of the disease. Not that these cuffs are the accompaniment of encephalitis alone (they are also found in trypanosomiasis and in paresis), but they are more developed in von Economo's disease than in any other. On the other hand, cellular lesions properly so-called are of secondary importance. Neuronolysis and neuronophagia are either discrete or absent in the whole of the mesencephalon, except in a well defined zone, the locus niger, as was shown at the outset by Marie and

81. Vide paper published by Castaigne and Cathala in J. méd. franç., Paris **9**: 124, 1921.

Trétiakoff,[82] and even here they do not occur in all cases. But, even on this level, neuronophagia does not present the same appearance as in poliomyelitis. The invasion of the nerve cell by the polymorphonuclear cells, which is so intense in poliomyelitis, is almost completely absent in encephalitis. In the latter, it is the mononuclear cells which play the principal part as scavengers and as agents for the reabsorption of the pigmentary and other remains of disintegrated cells.

In a word, the lesions are of a definitely infectious character in infantile paralysis, and the alterations result rather from a chronic process in encephalitis. The latter only present a manifestly acute appearance in experimental animals—rabbits, guinea-pigs or monkeys. It is on this ground that the similarity of the two diseases becomes closest (parenchymatous encephalitis and polymorphonuclear cells; acute myelitis accompanied by neuronophagia with neutrophilic leukocytes in Heine-Medin's disease).

From the experimental point of view, the differences between the two diseases reside mainly in the unequal receptivity of the various animal species to the virus, as well as in the peculiarities of immunity and the properties of the serum. The poliomyelitis virus is pathogenic for the monkey and has little or no virulence for the rabbit or guinea-pig. The encephalitis virus, on the other hand, has little virulence for the lower simians, while it adapts itself so well to the rabbit that it is capable of turning into a genuine fixed virus. Experience shows, moreover, that active immunity, which can easily be produced with the virus of Heine-Medin's disease, is slow to appear and is rarely absolute in encephalitis.

These facts would be sufficient to establish a clear line of demarcation between the two processes. Harvier and I, however, feel that it would be useful to undertake a number of cross-immunity tests in order to make the distinction even clearer.

1. *Does the herpetico-encephalitic virus vaccinate against the virus of poliomyelitis?*—*Macacus cynomolgus* 41 was given 4, 6 and 6 cc. of fresh encephalitis virus under the skin on March 17, 23 and 29, respectively. On April 10, poliomyelitis virus preserved in glycerine was inoculated into the brain. On the fifth day, there appeared general trembling and facial paralysis. Death ensued from typical poliomyelitis on April 10.

The conclusion is that herpetico-encephalitic virus does not vaccinate the monkey against the poliomyelitis virus.

2. *Does the virus of infantile paralysis vaccinate the rabbit against that of encephalitis?*—Two rabbits, 36A and 37A, were given, under the skin, 5 cc. of virulent emulsion of the marrow of a monkey with poliomyelitis on April 20 and 26. On March 5, these animals were tested by the cerebral route with an emulsion of encephalitis virus. They died on May 9 and 10 (i. e., after four and five days, respectively) with intense lesions.

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82. Marie, P., and Trétiakoff, C.: Bull. et mém. Soc. méd. d. hôp. de Paris **42**:475, 1918.

These experiments, showing as they do the absence of any cross-immunity between the virus isolated in epidemic encephalitis and that of poliomyelitis, demonstrate the different nature of the two viruses.

Harold Amoss [15] has confirmed these data. He showed that the serum of patients (human and simian) who had recovered from poliomyelitis neutralizes the virus of Heine-Medin's disease (Levaditi, Landsteiner, Netter), whereas the serum of those recovering from encephalitis has no neutralizing properties so far as the aforesaid virus is concerned.

Harvier, Nicolau and I endeavored to determine whether the poliomyelitis virus, when injected into the cornea of the monkey, produces the disease and gives rise to a keratoconjunctivitis similar to that caused by the virus of encephalitis. The result of our research work is as follows:

It is impossible to produce poliomyelitis in the monkey and in the rabbit by inoculating the *cornea* with passage poliomyelitis virus. Such inoculation is, moreover, followed by no local reaction.

Experiments.—1. Poliomyelitis virus preserved in glycerine was inoculated intracerebrally into *Macacus cynomolgus* 13. The animal developed paralysis on the seventh day and died of poliomyelitis on the eighth. Its brain was used to prepare a thick emulsion which was inoculated into the cornea of *Macacus cynomulgus* 10. The animal showed no local reaction and survived. Nevertheless, it was sensitive to poliomyelitis virus, for, being inoculated with this virus by the cerebral route on the fifth day, it developed paralysis and died on the sixth.

2. The brain of this monkey was used to inoculate *Macacus cynomolgus* 12 by the corneal route. The animal survived without any signs of local reaction.

3. Material from the same brain was inoculated into the right cornea of rabbits 83-0 and 88-0. Slight striae were visible on the next day, but no keratitis developed during the ensuing days. The animals survived.

These experiments show that, unlike the rabic and encephalitic virus, the poliomyelitic virus has no affinity for the corneal epithelium.

Epidemic encephalitis and epidemic poliomyelitis are two etiologically different infectious processes, although they are caused by ultraviruses belonging to the same group of neurotropic ectodermatoses.

News and Comment

THE UNITED STATES VETERANS' BUREAU NEEDS PHYSICIANS

Anticipating the need of physicians in the future, the U. S. Veterans' Bureau proposes to place on duty at its several hospitals throughout the United States thirty additional physicians as soon as they can be secured. These physicians must meet the requirements of the Civil Service Commission as to training and experience; in general, it may be stated that they must have graduated from a class A medical school within five years of date of application and, in addition, must have had at least one year's internship in a general hospital.

Physicians who have had training and experience in such specialties as neuropsychiatry, operative surgery, eye, ear, nose and throat diseases and clinical pathology, are particularly urged to forward their applications to the U. S. Civil Service Commission, 1724 F Street N. W., Washington, D. C., and request that the necessary forms be sent them for execution.

The medical service of the bureau offers a diversified and interesting service for physicians, with opportunities for research, postgraduate training, etc. The entrance salary is $3,200 per annum, and, if the service of the medical officer is satisfactory, he may be promoted in increments of $200 per annum; on the completion of three years' satisfactory service, he will automatically be promoted to the next higher grade at the minimum salary of that grade, $3,800 per annum.

POSTGRADUATE STUDY IN NEUROLOGY AND PSYCHIATRY IN VIENNA

A six weeks' course in neurology and psychiatry and associated branches will be given between Jan. 2 and Feb. 15, 1930, inclusive. Applications should be sent to Docent Dr. E. Spiegel, Falkestrasse 3, Vienna I, Austria.

FIRST INTERNATIONAL CONGRESS ON MENTAL HYGIENE

The First International Congress on Mental Hygiene will be held in Washington, D. C., May 5 to 10, 1930. It is sponsored by mental hygiene and related organizations in more than twenty-six countries. The honorary president is Herbert Hoover, the president Dr. William A. White, Washington, D. C., the secretary-general Clifford W. Beers. Address inquiries to the administrative secretary, John R. Shillady, 370 Seventh Avenue, New York.

Abstracts from Current Literature

AXONAL SWELLING OF THE PURKINJE CELLS, ESPECIALLY IN SENILE DEMENTIA. L. BOUMAN, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:379 (March) 1928.

Axonal swelling of the Purkinje cells has been described in many instances. Sträussler (1906) first called attention to axonal swelling in a case of congenital cerebellar atrophy. He later found it also in juvenile paresis and in the Spielmeyer form of amaurotic family idiocy. Schaffer also called attention to the local swelling of the axons in amaurotic idiocy. Bouman found axonal swelling in 100 per cent of cases of senile dementia.

Histologically, Sträussler (1906) found swelling of the axons in a case of cerebellar atrophy, in addition to swelling of the dendrons; the axonal swelling was not as marked as that of the dendrons. He later found similar changes in cases of juvenile paresis and concluded that this condition was a developmental disturbance. Rossi (1908) found changes in the Purkinje cells in a case of cerebellar sclerosis. He found a disappearance of Purkinje cells and a decrease in volume and dendrons in such of these cells as remained. Nageotte and Kuidberg (1908) described spindle-like swellings in the axis cylinders of Purkinje cells in two cases of cerebellar atrophy, and in two other cases in which the cerebellum was morphologically unchanged but in which the patients showed disturbances of motion. Laignel-Lavastine and Pitulescu found small enlargements on the end of certain axons in six paretic cerebellums. These "Kugeln" stained rather characteristically and were more numerous in the granular layer of the cerebellar hemispheres. They later found new enlargements, not only in the latter place, but also in the molecular layer of the vermis and in the granular and molecular layers of the hemispheres. These enlargements were more numerous the more intense was the meningeal reaction. As a rule, they lay parallel with the surfaces of the lamellae. In a case of cerebellar tumor, Marinesco and Minea (1910) found Kugeln in the granular layer, and were able to trace these in several instances to the axons of Purkinje cells. The axis cylinders ended for the most part in an ovoid or fusiform swelling. Similar observations were reported in a case of acoustic tumor with compression of the cerebellum, and also in a case of cerebellar softening. Schroeder (1911) reported axonal swelling of the Purkinje cells in a case of dementia praecox. Alzheimer (1912) found this sort of pathologic process infrequently in amaurotic idiocy. He found it frequently, however, in the cerebellum in paresis, juvenile paresis, tuberculous meningitis of adults, and fairly often in cerebellums with foci and in diffuse atrophy of various sorts. Schaffer (1911) found two sorts of axonal swelling in amaurotic idiocy — a local volume increase in the axoplasm, and a dark homogeneous nodosity. In a case of so-called pellagra typhus, Rossi (1913) found the axons of Purkinje cells ending often in Kugeln, and Bielschowsky (1914) found balllike swellings on the axons of Purkinje cells in the late infantile form of amaurotic idiocy. Cajal (1914) mentioned the swelling and branching of the axons of Purkinje cells in various nervous diseases. Doinikow (1915) found similar changes in the Purkinje cells in multiple sclerosis, and Bielschowsky (1918) in five patients with juvenile paresis. Bouman (1918) found axonal swelling (torpedoes) in many cases, chiefly in senile dementia, but also in arteriosclerosis cerebri, Huntington's chorea and general paresis. Schaffer (1922) and Globus (1923) found similar changes in Tay-Sachs disease. Schob (1923) reported axonal swelling of the Purkinje cells in acute multiple sclerosis.

Bouman investigated the cerebellar hemispheres in all patients with senile dementia and, using the Bielschowsky stain, he found axonal swelling of the Purkinje cells in every case (sixty-seven) except two. In these two cases the sections did not stain well and other material was not available for further study. He called the swelling at the end of the axis cylinders "torpedoes," because of their resemblance to torpedoes. Their structure was the same in every instance.

In most cases they were shaped like spindles, and their greatest width was about four sevenths of their length. They stained a sort of violet tint with Bielschowsky stain. They were homogeneous in structure in their interior, but had a netlike structure at the periphery. They lay mainly in the uppermost fluid of the granular layer. Variations of this structure occurred, but were less frequent in the cases of senile dementia than in other diseases. Bouman stated that he believed that axonal swelling of the Purkinje cells in the cerebellum in senile dementia is a constant microscopic observation. Senile plaques were found in the cortex in most cases of senile dementia with the foregoing manifestations; while these swellings or torpedoes occur constantly in senile dementia, they occur also in other diseases — arteriosclerosis cerebri, atrophy of the frontal lobe, general paresis, juvenile paresis, tabes, acute disseminated encephalitis, multiple sclerosis, cerebellar sclerosis, tuberculous meningitis, uremia, congenital cerebellar atrophy, Huntington's chorea, imbecility, idiocy, epilepsy, dementia praecox melancholia and manic-depressive psychosis, and experimentally in a section between the Purkinje cells and the dentate nucleus. The question arises as to the cause of these axonal swellings. As they may occur by interruption of the axon experimentally, it would seem that they result in man from a lesion interrupting the axon. This is not always the case, and the only conclusion that Bouman was able to reach with regard to their etiology was that they may be produced by a variety of causes. The torpedo formation or axonal swelling must then be conceived as a reaction of the neuron or axon to any sort of an outside noxious agent, represented by the various causes which have already been detailed. Bouman stated that the formation of the axonal swelling in senile dementia is due to a change within the neuron itself.

Many theories have been offered to explain the occurrence of axonal swellings of Purkinje cells. Cajal observed such swellings following interruption of an axon experimentally and also in the cerebellum of a new-born child or in a child that had died a few days after birth. He concluded, therefore, that these protoplasmatic clumps of juvenile axons represented reserve material for the formation of collaterals or the growth of axis cylinders. Nageotte pointed out that these swellings occur on the axon at a certain point, before collaterals are given off. Marinesco and Minea agreed with Cajal that the swellings represent sources of secondary ramifications of the axons. The swelling of the axons, the swelling of the fiber and the hypertrophy of the intracellular neurofibrils are looked on by most authors as either a degenerative or a regenerative process.

ALPERS, Philadelphia.

CENTRIFUGAL INFLUENCE OVER THE CENTRIPETAL SYSTEM IN THE CENTRAL NERVOUS SYSTEM. B. BROUWER, Deutsche Ztschr. f. Nervenh. **105**:9 (Sept.) 1928.

In an investigation of the structure of the central optic systems of higher mammals, Brouwer observed that in the brain of the rabbit and the monkey, centrifugal tracts originate which end in the lateral geniculate body, a center considered as an exclusive end-station for centripetal associations.

Brouwer refers to experimental work which he performed in association with W. P. C. Zeeman, and reported in 1926 before the Congress of the German Neurological Society. They showed that circumscribed retinal lesions in the rabbit, cat and monkey cause circumscribed secondary degenerations in the entire primary optic neuron. The retina of these animals is projected in the lateral geniculate body in a definite manner, and, in the rabbit, also in the anterior corpora quadrigemina. The projected upper quadrant of the retina is medial and the lower quadrant lateral in the lateral geniculate body. The macula sends some fibers to the middle and its largest number to the dorsal part of this ganglion. The macular field therefore partly separates the dorsal and ventral peripheral corneal quadrants. A part of the peripheral corneal quadrant must be represented in the most ventral part.

These investigations, by the Marchi method, permitted only the study of a pure centrifugal neuron degeneration. In order to study the retinal projection on the

cortex, Brouwer, with G. J. Van Heuven, produced various circumscribed lesions in the area striata of nine monkeys, causing a retrograde degeneration in the lateral geniculate body. The animals were kept alive for about eight months. Since the various retinal areas as represented in the geniculate body had been demonstrated through the previous experiments, the degeneration in the geniculate body caused by lesions in the area striata enabled the authors to learn the retinal projection in the area striata.

As a result of these experiments Brouwer comes to the conclusions: (1) That part of the area striata in the monkey which lies lateral to the cortex surface must be considered exclusively as the association of the macular end-station, although the macular field undoubtedly extends further over the area striata. (2) This retrograde degeneration affects also the large cells which are found in the ventral border of the external geniculate body. This group of large cells is not as prominent in the monkey as in man, yet they are always to be found. Reported observations on occipital lesions in man have repeatedly stated that the cells suffer little, or not at all, from retrograde degeneration. This fact led to the idea that this part of the external geniculate body does not project on the area striata. According to the observations of Bouwer and his co-worker, it is definitely established that all cells of this ganglion send their axis cylinders to the cortex.

Interpreting these conclusions physiologically, they indicate that all optic stimuli which reach the lateral geniculate body from the tractus opticus are transmitted by the second neuron to a higher level. There are no cells in this ganglion which permit the centripetal stimuli to flow to a lower level, there to develop optic reflex movements. These lower optic reflexes must take place without participation of the geniculate body.

Study of the third neuron and the distribution from the area striata over the rest of the cortex was done by the author in association with A. Biemond. They produced circumscribed lesions in the occipital cortex of the monkey. After ten days, the animals were killed and the brains studied by the Marchi method. The lesions were made mainly in Brodmann's field 17, which in the monkey is found on the lateral occipital surface. These investigations disclosed that a part of the centrifugal systems connects with lower levels of the central nervous system. This was to be expected, as a corticofugal connection with the anterior corpora quadrigemina is well known. The outstanding observation was a fairly sized tract which passes down the fasciculus longitudinalis inferior and ends in the lateral geniculate body itself. So far, the author has found it only on the homolateral side. The fasciculus longitudinalis inferior, therefore, transmits stimuli not only from the lateral geniculate body to the area striata, but also in the opposite direction. This association shows a tendency for definite localization.

According to the author, the existence of a corticofugal connection with the lateral geniculate body must have a physiologic significance. The highest association center, the cortex of the brain, is thereby enabled to exert an influence over the activity of the primary optic main station. This influence must not be compared with the influence the cortex of the brain exerts over lower reflex centers in other parts of the nervous system, for it was shown that lower optic reflexes cannot take place in this ganglion.

The author suggests that the function of this centrifugal system is that of inhibition. The existence of a system which inhibits the primary centripetal centers was suggested by Brown-Sequard, Fabritius, and lately by O. Foerster, who assumes a corticofugal tract in the posterior lateral column of the cord, which inhibits the sensitiveness of the posterior horn cells as well as the pain conduction. According to Foerster, this corticofugal inhibitory tract probably also exerts an inhibitory influence on the gray nuclei in the formatio reticularis of the medulla. Such a tract has not yet been found, but the result obtained in the optic system makes it advisable to search for such centrifugal connections with primary sensory centers. The assumption of such a function in the optic system is justified only when the conception of inhibition is that of a superordinated system. Here the author approaches nearer to psychology. He refers to M. Straub's opinion that

psychologic conceptions cannot be dispensed with in lower reflexes. In learning something new, attention must not only be given to the proper stimuli but it must at the same time inhibit other stimuli. Such a functional interpretation Brouwer is inclined to give to the corticofugal connection described. In this manner the cortex of the brain is enabled to suppress the stimuli of some cells in the lateral geniculate body and to increase them in others.

BERNIS, Rochester, N. Y.

CONCERNING THE DIFFERENCE IN STAINING PROPERTIES BETWEEN THE PERIPHERAL AND CENTRAL PORTIONS OF THE DORSAL ROOTS. LEO ALEXANDER, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **30**:185 (Aug.) 1928.

Redlich has shown that there is a difference in staining properties between the intramedullary and extramedullary portions of the dorsal nerve roots of the spinal cord. According to his observations, the intramedullary portion stains darker with Weigert's myelin sheath stain than does the extramedullary portion. The actual point of entrance of the root into the cord (Obersteiner and Redlich's point) is not to be considered, for here the staining properties of the myelin are extremely variable. Here the myelin sheaths are at times entirely absent so that the longitudinal black lines are broken by white stripes.

According to Richter, who considers this question an important one, some authors have mistaken this difference in staining for a pathologic change and have used it in various explanations of the pathogenesis of tabes. While Richter agrees with Redlich that normal spinal cords may exhibit variations in the staining of the extramedullary and intramedullary portions of the dorsal roots, he disagrees with Redlich on which portion stains more darkly and believes that the former stains better than the latter. As will be remembered, Redlich holds the opposite view.

Spielmeyer believes that in tabes the degeneration first begins where the dorsal root assumes central characteristics (Redlich and Obersteiner's "locus minoris resistentiae to the causative agent"): He bases this conclusion on the difference in myelin sheath staining between the extramedullary and intramedullary portions of the dorsal root. This assertion is contrary to that of Richter who holds that these differences in staining properties occur also in normal persons.

Richter later stated that in spite of the fact that normal cords show a difference in staining between central and peripheral portions of the dorsal roots, there still is a basis for comparison. This basis is present when the section cuts both portions of the root in a strictly horizontal plane. In his work on the histogenesis of tabes he shows such a section where there were marked meningeal changes. In this section the central and peripheral parts of the root stained alike, while the point of Redlich and Obersteiner plainly appeared as a white band.

In the present work Alexander shows that in normal subjects the extramedullary and intramedullary portions of the dorsal roots may stain alike, or the former may stain better than the latter, or vice versa. Further, he explains on what factors these differences in staining properties depend. He believes that the variability in staining depends not on actual structural differences in the portions of the nerve roots concerned, but represents merely a staining effect depending on the choice of varying concentrations of hematoxylin solution. This condition obtains throughout the entire vertebrate series; in previous works Alexander has shown that in certain marine animals the intramedullary portion of a dorsal root may stain lighter or darker than the extramedullary portion, or that both portions may stain alike.

The same variations can be produced in the human subject by variations in the staining technic. If the entrance of the hypoglossus is stained so that one portion is darker than the other, the difference can be seen under low power magnification, which shows the root in its entirety, as well as under high power magnification of the individual myelin sheaths themselves. (These facts are admirably demonstrated in the excellent photomicrographs accompanying the article—Abstractor's note.)

In order to answer the question of what concentrations of hematoxylin produce the various differences in staining, several pieces of adult human spinal cord were removed, fixed, hardened in Mueller's fluid and embedded in celloidin. These separate pieces were then sectioned parallel to the plane of entrance of the posterior roots. Continguous sections from each series were stained first for the same length of time with 1 per cent chromic acid and then treated with different concentrations of Weigert's hematoxylin solution.

The results were as follows: If a concentrated solution of hematoxylin was used, the intramedullary portion of the posterior roots stained more darkly than did the extramedullary portion. If a continguous section was stained with only a 20 per cent concentration of hematoxylin solution, the extramedullary portion of the root appeared darker than did the intramedullary portion. The same effect was produced if the sections were transferred from the water to the dye together with the strips of paper used to identify them. In this case the water contained in the paper diluted the dye coming in contact with the surface of the cut sections. If the sections were treated first with concentrated hematoxylin solution (after strong counterstaining with 1 per cent chromic acid) and then, without counterstaining again, differentiated and restained in another concentrated hematoxylin solution, the intramedullary and extramedullary portions of the posterior roots stained with similar intensity.

Alexander explains all the described phenomena by the difference in speed with which the extramedullary and intramedullary portions of the root take the dye in staining and give it up during the process of differentiation. These differences in staining properties of the two portions of the dorsal root correspond to chemical differences between the structures. These can be better understood when it is remembered that the myelin sheaths of the intramedullary and the extramedullary portions are of different embryologic origin.

As much pathologic significance is assigned to differences in staining of the myelin sheaths in various parts of the central nervous system, Alexander believes the subject to be worthy of further consideration.

KAMMAN, St. Paul.

THE MICROSCOPIC ANATOMY OF THE SECOND CASE OF PELIZAEUS-MERZBACHER DISEASE. MAX LIEBERS, Ztschr. f. d. ges. Neurol. u. Psychiat. **115**:487 (July) 1928.

The microscopic anatomy of Pelizaeus-Merzbacher disease, or so-called aplasia axialis extracorticalis congenita, is known only through the description of the first case in Merzbacher's monograph, and by a short report by Spielmeyer of the brain and cord in the second case, that of a sister of the patient in the first case. Other cases are reported in the literature, but these differ both clinically and histologically from the syndrome described by Pelizaeus-Merzbacher. These cases lack a hereditary history which, according to Merzbacher, is one of the most important factors in the disease. It is a markedly hereditary familial disease.

Pelizaeus first published his clinical description in 1895, and since then the disease in his patient has been followed through four generations, the healthy female always handing it on to her sons. Of the fourteen known cases, only two occurred in females; one of these is the case of Liebers. In his patient, the disease began typically in the third or fourth month, with shaking of the head and eyes. There then followed slowly increasing spastic contracture of the upper and lower extremities with a Babinski phenomenon, expressionless facies, nystagmus, scanning speech, tremor and choreo-athetotic movements. As the result of increasing contractures, and an osteoporosis of the bones with deformity of the shoulder girdle, paralytic-like states occurred which made the patient bedfast. Sensory disturbances were not observed and intelligence suffered but slightly. Death occurred as a result of an intercurrent infection of the lungs.

Macroscopic examination of the brain showed no abnormalities save that the gyri were somewhat smaller. Frontal section showed marked atrophy of the

entire white matter which was noticeable chiefly in the decreased size of the gyri. This was most marked in the frontal, temporal and occipital areas. The centrum semiovale and corona radiata were also markedly atrophied. The U fibers were normal. The corpus callosum was decreased in size; the subcortical ganglia were grossly normal. In the atrophied areas of white substance, which had a gray-blue appearance, were small islands of a yellowish-white appearance which corresponded to areas of normal white matter scattered here and there in the diseased areas. These gray-blue areas were seen in the pons and midbrain in the region of the medial fillet and cerebellar peduncle. The white matter of the cerebellum showed the same condition as that of the cerebrum.

Microscopically, the most important characteristic of the disease is an atrophy chiefly in the central white matter of the cerebrum and cerebellum with maintenance of the normal configuration of the brain. The atrophy is accompanied by disappearance of the myelin sheaths. On the other hand, as Spielmeyer pointed out, there is also partial degeneration in the cortical gray and central gray, in the basal ganglia, pons, midbrain and cortex. The medulla and cord show degeneration not only in the white but also in the gray matter. The picture in the cortical white matter closely resembles diffuse sclerosis, with the difference that in Pelizaeus-Merzbacher disease there are scattered islands with normally preserved myelin sheaths within the areas of atrophy. These islands appear as dark points and give the tissue a tiger-like appearance. The islands are regularly scattered about, and are without recognizable relation to definite fiber tracts and systems. The arcuate fibers and Meynert's U fibers are practically intact. In the cortex the tangential fibers are practically gone, and the radiary, interradiary and superradiary fibers are either markedly fewer in number or have little myelin covering. The areas of the cortex best preserved are the central convolutions, the area striata, cornu ammonis and hippocampus. The lines of Gennari in the area striata stand out particularly well. Bielschowsky preparations show that the axis cylinders are still present in the atrophied areas. The islands of myelinated fibers, seen in the areas of atrophy, more or less lose their significance because on microscopic examination a number of small well stained islands are found with myelin sheaths intact, and, furthermore, a large number of larger and pale blue-gray stained islands — so-called "Markschattenherde" of Marburg and Spielmeyer. Besides these there are seen bundles of blue-gray, weakly stained myelinated fibers, and scattered solitary fibers with well preserved myelin sheaths scattered here and there in the atrophied areas. Fat stains show that the pathologic process consists of a definite but slow process of degeneration. The glia cells often show fine fat droplets about their nuclei. Granular cells are seen in the perivascular spaces. Free fat is found in the adventitial lymph spaces and in the lumina of the vessels. On the whole, this is a slowly progressing "Abbau" process. Lymphocytes and plasma cells are entirely lacking.

A comparison of the case reported by Liebers with the first case reported by Merzbacher shows that the pathologic process is the same in both cases, the difference being merely quantitative. It is important to note that in neither of these cases was there any involvement of the cells in the cortex, so that a cellular cortical origin of the axial atrophy in these cases is out of the question. Pelizaeus-Merzbacher disease is a hereditary endogenous disease with no aplasia, but with a chronic slowly progressing degenerative process of the white matter, with glial overgrowth and relative intactness of the axis cylinders.

ALPERS, Philadelphia.

SUBOCCIPITAL PUNCTURE. V. SCHMIEDEN and H. FISCHER, J. f. Psychol. u. Neurol. **37**:303, 1928.

Suboccipital puncture is indicated in all intracranial conditions in which there is an increase of spinal fluid or a disturbance in its circulation. Its effect is the same on the subdural as on the intraventricular fluid system. It is especially indicated in conditions in which it is necessary to withdraw fluid during a pro-

longed period from the cerebellomedullary system and from the fourth ventricle. The only dangerous feature of the method lies in the possible untoward effects following the sudden release of intracranial pressure after the rapid withdrawal of the fluid. This, however, can be obviated by allowing the fluid to drain off slowly and gradually by cisternal puncture through a wide opening in the atlanto-occipital membrane while the patient is in the recumbent posture and the upper part of the body is slightly elevated. In many cases, suboccipital puncture is followed by the formation of a spinal fluid cyst in the soft parts of the neck; this gives rise to a sort of fifth ventricle which may be regarded as an artificial sub-occipital meningocele that frequently serves to establish a normal equilibrium to the spinal fluid pressure. In unusually severe cases of hydrocephalus, frequent puncturing of these artificially formed cysts will be followed by the formation of new channels within the surrounding soft parts and the vascular system for further drainage of the fluid.

The passing of sounds through the cisternae and fourth ventricle during the operation has in numerous instances been an effective method for the production of good drainage. This part of the technic is absolutely free from danger and permits the formation of a new opening in the membrana tectoria which therapeutically has the same effect as a patent foramen of Magendie.

The indications for suboccipital puncture are: cerebral growths, hydrocephalus, serous meningitis, epilepsy, migraine and acute and tuberculous meningitis.

In cerebral neoplasms the method may be regarded as a palliative operation. For the successful outcome of any operation for cerebral neoplasm a free communication between the cerebral ventricles is a sine qua non. Such communication can best be obtained by suboccipital puncture which, in a majority of cases, is followed by a rapid disappearance for a considerable period of the distressing general symptoms of increased intracranial pressure. Improvement is thus registered by the regression of the papilledema and a favorable effect on the other neurologic symptoms. Not infrequently, the disappearance of the general symptoms of tumor of the brain may so affect the entire clinical picture that one may be enabled to make a topical diagnosis of a focal lesion the localization of which had previously been impossible. The relief of increased intracranial pressure as a preliminary measure prior to removal of a tumor is always desirable and can best be accomplished by suboccipital puncture.

In hydrocephalus, suboccipital puncture must be resorted to as early as possible. The ideal time is before the increased intracranial pressure has produced atrophy of the cerebral hemispheres. To obtain the best results it may be necessary to combine suboccipital puncture with callosal puncture. This is especially the case in unusually severe forms of hydrocephalus.

In the traumatic, toxic and infectious types of serous meningitis, suboccipital puncture is followed by excellent results owing to the permanent release of pressure following the operation. Chronic serous occipital meningitis, in which the disease has produced membranous adhesions in the region of the fourth ventricle followed by diaphragmatic closure, is especially favorably affected by this procedure.

In epilepsy the formation of a cyst, following suboccipital puncture, is helpful in aiding the normal regulation of the intracranial pressure; this in itself removes the vicious circle, diminishing thereby the tendency to convulsions. The same may be said of migraine, especially when it is associated with an increased secretion of spinal fluid, as in Quincke's edema.

In the treatment for purulent meningitis, suboccipital puncture is indicated in recent cases in which good drainage of the infected fluid for a more or less prolonged period is absolutely essential.

The good effects following suboccipital puncture in tuberculous meningitis are due to the release of cerebral pressure and the evacuation of the exudate, following which, as in tuberculous peritonitis, certain chemicobiologic reactions occur which seem to have a favorable effect on the pathologic process.

KESCHNER, New York.

OBSERVATIONS IN OLD CASES OF SCHIZOPHRENIA. U. FLECK, Arch. f. Psychiat. **85**:705 (Nov.) 1928.

The purpose of the work was to determine the influence that age and a prolonged, practically uninterrupted confinement in a hospital for mental diseases would have in cases of schizophrenia. The material consisted of forty patients who had been in the hospital for more than twenty years. The present communication, however, is restricted to conclusions that could be drawn out of a study of seventeen of these patients who were 65 years of age and over. The author appreciates the fact that this material is not altogether representative of the average schizophrenic patient. Patients whose conditions are more serious, who tend toward early emotional and intellectual deterioration and are, therefore, rather difficult problems for care, do not as a rule reach such an advanced age. Furthermore, the patients studied were all of the male sex. Within these limits, however, he thinks that certain conclusions can be drawn as to the effect of these conditions on the course of a schizophrenic psychosis. With the exception of a few cases, the history, onset and progress at the hospital are described fairly fully for each patient. At the beginning, all the patients showed a picture complex which, without doubt, fitted into the diagnosis of schizophrenia. In most cases, the psychosis was of a serious degree, frequently of the type that shows acute exacerbations with gradually progressing mental deterioration in the intervals. This deterioration (if it could be called such), however, was more in evidence during the earlier years of the stay at the hospital. The tendency to acute outbreaks such as stupor, excitement, emotional instability and so on, as well as the hallucinatory and delusional trends, seemed to subside as time went on. Strange as it may seem, even the apparent defect which was noticeable in the intervals between exacerbations in the early stages seemed to become less marked with years. In some cases, for instance, when attempts at allowing the patients to go out on short visits were unsuccessful in the earlier stage, the patients were able to spend short periods of time outside and even to take longer or shorter trips from the hospital without getting into difficulties many years after the onset of the psychosis. Actual symptoms of a senile psychosis do not seem to have developed in any case, and definite arteriosclerotic manifestations were present in only one case. On the basis of these observations the author comes to the conclusion that, in some cases of schizophrenia, the changes concomitant with advanced age (not necessarily psychotic) influence favorably the acute symptoms of the psychosis. The explanation for this rather unexpected occurrence could be looked for on the basis of different theories. In some cases the author would agree with Hoffmann, who is of the opinion that in normal, as well as in pathologic, personality traits a great change may occur from the biologic effects of involution and senium. According to Hoffman these may bring about a cropping up of incompatibilities in previously well adjusted personalities, on the one hand; on the other, however, they may condition a smoothing out of emotional and instinctive disturbances and lead to a more harmonic and milder outlook and adjustment. In the latter, early pessimistic hypochondriac, emotionally unstable tendencies may give place to a mellow, optimistic and in some cases even a euphoric outlook on life. This is encountered not only in so-called normal persons, but also in those lying without the normal limits. Another possibility to be borne in mind is that with the involution of some of the endocrine organs, inabilities of adjustment conditioned by these necessarily lose in importance, and the prepsychotic traits of character may come to the surface again. There is no question but that the environment plays a great rôle in shaping the behavior of these patients. The sheltered life at the hospital and the lack of disturbing elements in the environment, as well as the relief from independent and responsible activity, contribute a share in causing the gradual adjustment to conditions.

MALAMUD, Foxborough, Mass.

RELATION OF MEDICINE TO PSYCHOLOGY. JOSEPH JASTROW, J. A. M. A. **92:** 720 (March 2) 1929.

The claim of possession, that the body has a mind or that the mind has a body, is as misleading as the allied doctrine of demon possession, the first encounter of physician and psychologist. The physician of today is referred to by the author, who is Ph.D. and LL.D., not M.D., as the "twentieth-century limited" physician, who, when confronted with a mental case says, "Let George the psychologist do it," and the latter is easily flattered into the ambition to be all things to men and even more to some women, whom it is more interesting to psycho-exorcise. There should be no division of human behavior into bodily and mental behavior. Hygiene and pathology, sanity and insanity, behavior and misbehavior, are only phases of the same vista.

There follows the relation of anecdotes concerning a Neapolitan physician, Jerome Cardan (1501-1576), and another concerning a Justice Holt (1642-1710) illustrative of the credulity and magic of that day. The problem of drug action and that of psychic poisons influencing physiologic behavior illustrate the joint interest one focused in medicine, the other in psychology. To deny either leads to Christian science, absent treatment and the absurdities of addled thinking or to the evils of all sorts of "patent medicines." The drug addict and the psychic addict offer comparable and overlapping problems. The hell of slavery to drug addiction has been produced by the same route that has brought anesthetics, asepsis, quinine and insulin.

If the thyroid is the miracle gland, it is because of the discovery that supplying its deficiency converts the feebleminded cretin into a near normal. Dr. Cannon in his work on fear and rage has contributed to psychology as directly as to medicine. While one can allay nervousness by so doing, one cannot inject courage and calm into the veins and secretions any more than one can find a drug to make men truthful. Nature provides for complexity of behavior through the double route of the autonomic nervous system and the craniospinal system.

The dominance of the emotional reactions must now be recognized. One does well, says the author, "to recognize the freudian formula" based on the psychogenic production of incapacities and interferences with normal bodily functions. Freud has provided a powerful microscope, if properly adjusted, for the analysis of human behavior. Maladjustment on a basis of thwarted and strident sex urges has become truer by freudian emphasis and by exaggeration. There is no more cogent example of the interpenetrating territory of medicine and psychology than the freudian movement. Psychoanalysis, however, is but one application of freudian psychology, and the freudian procedure is but one form of analysis.

This is the psychoneurotic age, and the psychoneuroses are increasing. There must be an effort to control this condition. It requires understanding and instruments of control. Only one of every five or ten hysteric, neurasthenic, psychasthenic and psychopathic personalities seeks medical aid. The author suggests for these people, who are handicapped rather than crippled and who do not know where to turn, a "misery clinic" in which physician and psychologist cooperate to the fullest extent and avoid the result that the patient is made a victim of some quack, having been assured that he is physically sound and this assurance, of course, being unsatisfactory.

The author would add to the board of consultants mentioned social workers, laymen and laywomen. The conditions of patients would be diagnosed, treated and followed up to consummation.

CHAMBERS, Syracuse, N. Y.

THE GENERAL PROBLEM OF OCULOGYRIC CRISES IN THE COURSE OF CHRONIC EPIDEMIC ENCEPHALITIS. RENE DELBEKE and LUDO VAN BOGAERT, Encéphale **23:**855 (Dec.) 1928.

When symptoms following encephalitis began to be described it was natural that one of the most bizarre complexes should assume prominence, i. e., oculogyric spasms. Later, it became evident that there were associated states — extreme

anxiety and anguish, loss of vision, definite increase of hypertone, etc. — accompanying these attacks. Then Falkiewicz and Rothfeld described a case in which the crises came on under the influence of psychic excitations. Out of all this has come the point of view of regarding the ocular symptoms as merely the most visible element in a complex paroxysm. These symptoms may be grouped as neurologic (extrapyramidal and postural), vestibular, vegetative and psychic.

In the past three years, the authors have studied a series of twenty-five cases. Seven of these are described in the paper. The authors comment on the observation that there is often transitory pupillary rigidity, coinciding in time limits to the occurrence of the spasm. All sorts of labyrinthine alterations have been reported — inconstant and irregular — and such that they cannot be considered as a primary symptom of the oculogyric crisis, but rather as "secondary symptoms of resonance." It is felt that all this points to a disturbance of the supranuclear control system, in the way of either excitation or blockage. The occasional presence of labyrinthine and neck reflexes speaks in favor of a pathologic excitation of the posterior longitudinal bundle.

Other occasional symptoms are: disturbances of mastication, of deglutition or articulation, echopraxia, trembling, tachycardia with hypotension, respiratory alterations, augmentation of the secretions, etc. On the sensory side there may be complaints of itching, tingling, pains in the eyes and similar sensations. A long case history describes a transitory hemianesthesia; in another, the patient had definite visual hallucinations. On the psychic side, cases may be classified into three groups of syndromes: of anguish and anxiety; of obsession, of psychic inhibition. The first mentioned often initiates the entire attack, or it may be an isolated phenomenon. The obsessions described are typical of those in so-called psychoneurotic patients; the psychic inhibitions are of all grades up to complete loss of consciousness. These various mental representations can at times completely substitute for the crises.

The mooted question of the inter-relationship of organic and psychogenic is entered by the writers, with a firm conviction that underlying it is a real neurologic basis. Although the psychic influences are undoubted, these act on a structure "authentically neurologic." Pharmacologic experiences, in which the patients showed some improvement under administration of calcium, benzyl benzoate, atropine and the salicylates, are given in detail.

Finally, they give a long discussion of the relation of processes of excitation and inhibition, showing the importance of the idea of sleep as an internally inhibited reflex. Many of the states are similar to those of catalepsy, and this is viewed as a normal and constant reflex, which is not ordinarily manifested because of the suppression of the influence of the hemispheres.

ANDERSON, Kansas City, Mo.

PSYCHIC CHANGES IN TUBERCULOUS CHILDREN. T. P. SIMPSON, Collected Papers, Psychiatric Clinic of the First Moscow State University **2**:71, 1927.

The extensive literature dealing with the personality changes in tuberculous children is reviewed by the author. Two groups of children were studied. The first group consisted of 158 children with bovine tuberculosis and also with a scrofulous diathesis who were living at home and were attending a fresh air school. The second group consisted of forty children with pulmonary tuberculosis in a sanatorium. The children were studied in great detail by physicians, psychologists, sociologists and school teachers. Anthropologic studies were done according to Kretschmer's classification. Medical studies included the use of fluoroscopy, the x-rays, various biologic reactions and blood tests. The psychologic studies consisted of measurements of intelligence, association tests, analysis of dreams and an analysis of behavior charts in school and at home. Heredity was studied back for four generations, and the ancestors were classified in accordance with Kretschmer's conception of personality types. Seventy-six per cent of the families were essentially cyclothymic; 16 per cent, schizoid, and 8 per cent, mixed. In 47 per cent

of the cases there was a history of mental disease in one or more ancestors. Anthropologic studies showed an asthenic type in 40 per cent of the cases. Dermographia, increased tendon reflexes and absence of conjunctival and corneal reflexes were observed in more than 50 per cent of the cases. There was usually fair intellectual development but marked reduction in attention and memory. The children were characterized by egocentrism, facility of speech and ease of verbal expression with rather shallow brilliancy. The imaginative faculty was well developed. The artistic production of the children, as well as their dreams, showed a marked feeling of isolation from the rest of the world. In the affective sphere, the children were extremely sensitive and rather sentimental. There was a good deal of irritability with quick responses to various stimuli, but the responses lasted a very short time and became quickly exhausted. The reaction of fear was extremely common. As far as psychomotor reactions are concerned, the author found two sharply differentiated groups of the hyperkinetic and the hypokinetic types. The mechanisms described by Adler in connection with the feeling of physical inferiority were very common. A study of the personality of the children showed that 43 per cent had a schizoid personality, 20 per cent a cyclothymic and 11 per cent a psychopathic personality. There is a high degree of correlation between the severity of the disease and the personality type of the child. In the severe forms of intoxication the schizoid type of personality is most common. All these data refer to the children of the first group.

The children with pulmonary infections were studied with less detail on account of their condition. In most of the children, the author observed a marked psychomotor retardation. In this group there was commonly found a clinical picture suggestive of definite involvement of the central nervous system, so that some of the children looked as if they had a tumor of the brain or paresis.

The author feels that a tuberculous infection changes the personality of a child in the sense of "schizoidization" of the sick child.

KASANIN, Boston.

A CASE OF AMYOTROPHIC LATERAL SCLEROSIS AND BULBAR PARAYLSIS WITH PATHOLOGIC OBSERVATIONS. GEORGE ILBERG, Ztschr. f. d. ges. Neurol. u. Psychiat. **115**:423 (July) 1928.

Ilberg reports the case of a man, aged 46, who, during the cold weather incidental to service in the army, complained of a feeling of weakness in the legs with rheumatic-like pains in the legs. He lost power over his legs and fell down frequently. Muscular rheumatism and paralysis of the right arm developed. In 1918, at the age of 46, the tendon reflexes in the arms and legs were exaggerated, and a Babinski reflex was present on the left side. A diagnosis of hysteria was made. In the fall of 1918, there was deviation of the tongue to the right, loss of power in the back, atrophy of the right arm, weakness in both legs, a spastic gait with a bilateral Babinski sign, and an absence of abdominal reflexes. A diagnosis of amyotrophic lateral sclerosis was made. In 1920, the patient was worse, then showing disturbances in speech and swallowing, and atrophy of the muscles of the jaw, breast, arms, legs and shoulder girdles. Sensation was normal. The legs were spastic. Death occurred suddenly from asphyxia. A clinical diagnosis of amyotrophic lateral sclerosis with bulbar palsy was made.

Necropsy showed tuberculosis in the apex of the left lung and bronchopneumonia. The brain weighed 1,455 Gm. The spinal cord at all levels showed marked loss of cells in the anterior horns, only a few sclerotic cells remaining. The pyramidal tracts were completely degenerated in the lumbar segment, and only slightly less so in the thoracic and cervical levels. Degeneration was present also in the anterior columns, anterior roots and ventral part of the dorsal columns. Glial proliferation was marked in the degenerated areas, especially in the anterior horns of all regions. In the medulla, the hypoglossal nucleus was degenerated, and the roots of the nerve showed loss of myelin. The cells of the nucleus ambiguus were partially degenerated. Fiber degeneration was present in the restiform body, the spinal trigeminal root and the spinal vagoglossopharyngeal root. The root

fibers of the vagus were degenerated also. The pyramids were markedly degenerated. In the hind-brain there was loss of fibers in the posterior longitudinal bundle and the middle part of the median fillet. The facial nerve at its exit contained no myelinated fibers, and the abducens nerve also was much degenerated. The pyramidal tract here also was markedly involved. In the higher portions of the brain stem, degenerations were present in the pyramidal tract, in the posterior longitudinal bundle and lateral fillet, in the medial portion of the cerebral peduncles and in the internal and external capsules. The cortex itself showed a loss of cells and fibers in the frontal, precentral and first temporal areas. The precentral gyrus was smaller as compared with other gyri, and many ganglion cells were lost in the cortical areas mentioned. The case demonstrated a marked degeneration in the pyramidal tract system, with involvement also of other fiber systems.

ALPERS, Philadelphia.

CEREBRAL SUBCORTICAL SCLEROSIS OR SCHILDER-FOIX DISEASE. JULIEN MARIE, Ann. de méd. **24**:545 (Dec.) 1928.

To the many names which have been given to pathologic conditions resembling the original cases of "encephalitis periaxialis diffusa" of Schilder the author adds another suffix, the name of his master Foix. He attempts to classify the many cases published since 1912 into four groups, according to the duration of the pathologic process. The first three groups comprise the acute cases, and the fourth group the chronic type.

The author further differentiates the four groups according to the consistency of the brain tissue on anatomic examination. To the first group should belong cases that show grossly a soft brain which on histologic examination reveals numerous foci of necrosis. These foci are filled with compound granular corpuscles; their wall is formed by proliferating glia. The perivascular spaces are widened and filled with lymphocytes. As examples for this group are cited the second case of Schilder, and those of Henneberg, Stewart and others. To the second group those cases were added in which the brain tissue was harder than normal though intermingled with softer foci. Histologically, the areas of degeneration showed a marked formation of glial fibers intermingled with giant polymorphonuclear glia cells (cellules pseudogliomateuses). Schilder's case 1 and the observations of Bouman, Redlich, Neuburger and others make up this group. The third group is characterized by a hard consistency of the brain, which on cutting may be similar to rubber or gelatin. Macroscopically, atrophy of the white matter may be seen. Histologically, a marked glial sclerosis predominates; numerous compound granular corpuscles are found in the demyelinated areas. Perivascular infiltration may be absent. The cases described by Haberfeld and Spieler, Collier and Greenfelt, Brock and others belong to this group.

The fourth group comprises the chronic cases. The brain tissue is densified; the atrophy of the white matter is always marked, sometimes producing a sharp line of demarcation of the cortex. Histologically, the lesions present the picture of a dense meshwork of neuroglial fibers with numerous astrocytes. Compound granular corpuscles, giant glia cells and perivascular infiltration are absent. The cases of group 1 showed clinically the picture of a rapidly advancing disease with death after from two to several weeks. Group 4 is the end-stage of the acute forms and has probably passed through the other three different stages.

WEIL, Chicago.

TRAUMA AND PARKINSONISM. ANDREAS KLUGE, Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:1 (Nov.) 1928.

Owing to the fact that the war with all its injuries has caused no increase in the incidence of paralysis agitans, Reichardt and others have concluded that mental and physical trauma play no rôle of importance in the origin of paralysis agitans. Kluge says that the great increase in parkinsonism following epidemic encephalitis reopens the question of the relation of trauma to this disease and states that the onset of the disease often follows trauma. Reports in the literature are scarce.

The traumatic effects on the nervous system in the war have been studied carefully by van Schelven. He says nothing about the traumatic origin of paralysis agitans. Gierlich believes that 5 per cent of the tremors resulting from war injury are due to paralysis agitans. Busch reported sixty-six cases of paralysis agitans due to trauma up to 1914. He found trauma as a cause of paralysis agitans in 20 per cent of the cases at the Bonn clinic, and quoted other authors indicating that the incidence of trauma varied from 4 to 30 per cent. He says that trauma cannot cause paralysis agitans in a normal organism, but he concludes that "it can be assumed with absolute certainty, that there is a definite relation between paralysis agitans and trauma in many cases, and that indeed mechanical trauma is foremost in the direct causes of this disorder." Stiefler denies the importance of war injuries and calls attention to the common striatal component in hysterical neuroses, catatonia, multiple sclerosis, arteriosclerosis and paresis. Stürmer's case (1922) is of interest as showing a direct relation between trauma and the occurrence of a postencephalitic paralysis agitans. Of 146 cases, Patrick and Lewy found trauma in only twenty-two cases. Paulian (1922) reported four cases of parkinsonism due to trauma, but only one of these occurred in an encephalitis epidemic. Lambranzi also called attention to the rôle of both mental and physical trauma in the occurrence of parkinsonism. Maier's case is of great importance in this respect. He reported the case of a man, aged 45, who had had a severe trauma to the head ten years previously, but had no history of fever or disease, in whom parkinsonism developed five weeks after the trauma.

Kluge reports three cases of parkinsonsim which were directly related to trauma, and which he says demonstrate that trauma is a cause of parkinsonism.

ALPERS, Philadelphia.

DEATH FOLLOWING CISTERN PUNCTURE. PINEAS, Nervenarzt. **2**:25 (Jan. 15) 1928.

Comparatively few deaths following cistern puncture have been reported in the literature up to the present time, and it is for this reason that the author presents the following report. The patient was a man, aged 56, whose condition had been previously diagnosed as syphilis. Because of a negative reaction to tests of the blood and spinal fluid it was thought advisable to do a cistern puncture, to see if by any chance a different reaction might be obtained from this fluid. Accordingly, on Aug. 6, 1927, a cistern puncture was undertaken. The patient was placed in a sitting position, and the needle was inserted to a depth of about 6 cm. As no fluid was obtained, the needle was withdrawn and reinserted about 1 cm. under the previous puncture; at a depth of 5 cm. no fluid was obtained. With considerable care, the needle was inserted slightly deeper. Suddenly the patient collapsed, the needle was extracted immediately, and the patient placed in bed. The pulse was rapid and there was Cheyne-Stokes respiration. Efforts at artificial stimulation were instituted, but the patient died that evening.

At autopsy two small holes were found in the pia which covered the cistern. Directly under these puncture holes there was a vessel, about the size of a crochet needle, from which blood extruded. There was an extensive subpial bleeding which extended over the cerebellum and adjacent cord.

A careful histologic examination showed the blood vessels of the cord and stem to be chronically thickened and enlarged. Due to pial thickening, the cisterna magna was markedly altered in size, its usual large cavity being absent. From the examination it was not at all certain that the needle had entered the blood vessel, and it was suggested that there may have been a spontaneous rupture.

In conclusion, Pineas states that this was the first accident in 1,200 cistern punctures. He believes that undoubtedly no ill effects would have occurred in this patient from another lumbar puncture, but that as far as he was able to determine there was no contraindication to a cisternal puncture. He thinks that it is probably advisable to caution against the too free use of the cistern route and that it should be used only when indications are specific.

MOERSCH, Rochester, Minn.

A Contribution to the Study of Spontaneous Past-Pointing as a Cerebellar Symptom. Klestadt and Rotter, Arch. f. Psychiat. **84**:93 (May) 1928.

On the basis of a clinical and microscopic study of a case of their own and an analysis of the literature on this subject, the authors attempt to evaluate spontaneous past-pointing as a localizing criterion. The problem discussed is whether this sign should be looked on as merely indicative of general endocranial involvement, as pointing to an involvement in the posterior fossa or as a localizing cerebellar sign (according to Bárány). The case reported showed clinically spontaneous reeling forward and to the left, horizontal nystagmus both to the right and to the left and spontaneous past-pointing to the left. Injection of cold water into the left ear caused an attack of unconsciousness, with left-sided facial twitching, pronounced pallor and urinary incontinence. The autopsy showed a cystic tumor, the size of a walnut, in the lobus biventer and reaching to the lobus gracilis. The cortex was definitely affected, the white matter being somewhat compressed. Microscopically, there were neuroglial proliferations in both dorsal vestibular nuclei, white matter destruction in the lower olive and injury to the vestibulospinal tracts.

The authors discuss the following symptoms especially: (1) the spontaneous falling forward and to the left; (2) the horizontal nystagmus, and (3) the past-pointing. They do not consider the first symptom as pointing definitely to disturbances of the vermis, especially as no changes were found in the vermis. The nystagmus is regarded as due to irritations of the vestibular nuclei. The spontaneous past-pointing must have been caused by the cerebellar lesion. The lesion in the left cerebellar heimisphere could have conditioned the past-pointing by disturbances in the coordinating and tonic regulations. It is also possible that the disease of the vestibulospinal tracts, which convey the cerebellar regulation to the anterior horns, might have been responsible for the past-pointing. It must be regarded as well established that spontaneous homolateral past-pointing, especially when it is found in association with other cerebellar signs, points to a lesion in the posterior fossa.

Malamud, Foxborough, Mass.

South American Trypanosomiasis of the Meningo-Encephalomyelitis Type in New York. Russel G. MacRobert, J. A. M. A. **92**:**230** (Jan. 19) 1929.

A case of trypanosomiasis due to the South American type of flagellate parasite is reported. A woman, aged 36, came to New York in December, 1927, from Venezuela because of failing vision and extreme nervousness. Three ophthalmologists found vision of 6/200 in the right eye and 20/30 in the left eye. The right eye also showed dustlike membranous opacities and four retinal hemorrhages below the disk. The fundus looked hazy. The left fundus was slightly pale. Local or chronic infection, syphilis and pituitary neoplasm were suggested as possible causes. In February, 1928, the author was asked to make a neurologic examination, particularly regarding a pituitary tumor. X-ray plates of the pituitary region were normal. There was exaggeration of the deep reflexes; a rapid, marked flexor defense reaction occurred when the sole was stroked, but the plantar reflex was absent for both flexion and extension; the abdominal reflexes were absent. The visual fields were normal.

The patient was not seen again until April, when she was bedridden and seriously ill, and gave an interval history as follows: She had had a lumbar puncture with negative results. A few days later, a fever of 104 F. developed, which continued to a lesser degree for two weeks with respiratory symptoms; then she had become noisy and unmanageable and was thought to be suffering from a postinfluenzal major hysteria. She became worse and lay stiff in bed with frequent athetoid spasms of a rigid, tonic type. She could no longer speak English but only Spanish, and that was often unintelligible. There was slight fever, rapid respiration and rapid heart rate. She choked even on swallowing

fluids. The Babinski sign was bilaterally positive. There was now bilateral papilledema. The blood count yielded only a relatively high percentage of lymphocytes. The skin became bronzed. She became completely quadriplegic, aphasic and demented. She was taken home to Venezuela in September, 1928.

CHAMBERS, Syracuse, N. Y.

THE PROBLEM OF THE DIFFERENTIAL DIAGNOSIS OF NEUROSYPHILIS ON THE BASIS OF BLOOD AND CEREBROSPINAL FLUID EXAMINATIONS. A. FRIEDMAN, Arch. f. Psychiat. **84**:73 (May) 1928.

The author reports the results of serologic examinations in a large number of cases of different types of neurosyphilis and the conclusions that one can draw from these as to differential diagnosis. The tests used were as follows: Wassermann reactions of the blood and cerebrospinal fluid, the Manoiloff reaction of the blood, erythrocyte sedimentation reaction, the Takata-Ara reaction, the colloidal gold test, various globulin and albumin reactions, and cell counts. His conclusions were as follows: 1. The Wassermann reaction, in both the blood and the cerebrospinal fluid, is not reliable as, on the one hand, a number of patients otherwise definitely shown to have suffered from neurosyphilis showed a negative reaction, and, on the other hand, patients with tuberculosis, malaria, malignant tumors, recurrent fever, etc., can give a positive reaction without syphilis. 2. The Manoiloff reaction of the blood is much more reliable than the Wassermann reaction and is especially strong in tabes and in paresis. 3. The sedimentation reaction is definitely accelerated in all forms of active syphilis of the central nervous system, regardless of type. 4. One of the most reliable diagnostic criteria of metasyphilis is the new colloid reaction of Takata-Ara. Of similar importance, especially in differential diagnosis, is the colloidal gold reaction. 5. Cerebral syphilis and cerebrospinal syphilis show mostly a moderate pleocytosis with increased albumin, a characteristic colloidal gold reaction and a positive Nonne-Apelt test. In tabes, the Wassermann reaction is not always positive; as a rule, the pleocytosis is low and the colloidal gold curve lies between that of cerebral syphilis and that of paresis. In paresis there is a moderate or pronounced pleocytosis, characteristic colloidal gold and Takata-Ara tests and also characteristic albumin and globulin tests. 6. No single test is absolutely reliable, and should be considered only in conjunction with other tests. In most cases a repetition of the examination is necessary before a definite diagnosis can be made.

MALAMUD, Foxborough, Mass.

CEREBRAL TUMOURS. H. S. SOUTAR, Brit. M. J. **1**:53 (Jan. 12) 1929.

Tumors of the brain produce their effects by the interference they cause with the arteriovenous and cerebrospinal circulations. Added to the general effects of increased intracranial tension are the local signs depending on the location of the tumor. The mere pressure of a tumor on the actual cells of the brain would probably be entirely without results were it not for the interference with the cerebral circulation by which this pressure must in practice be accompanied. Congestion means irritation, anemia, paralysis. Interference with the circulation produces first congestion, then anemia surrounded by an area of congestion, and, perhaps every now and then, an acute edema may arise around the advancing tumor. There follows a consideration of the symptoms produced by lesions in various locations: the precentral gyrus with jacksonian attacks and paralysis; the intermediate precentral area with motor apraxia; the postcentral gyrus with sensory changes; Broca's convolution with aphasia; the visual tracts with hemianopic or quadrantic losses in the field of vision; the temporal lobe with its uncinate fits.

The vascular supply of the skull and of the scalp are entirely independent, so that the scalp may be turned down freely without the slightest prejudice to the vitality of an osteoplastic flap, which derives its vascular supply entirely from its muscular pedicle. In a temporal flap the anterior portion of the incision lies

well in front of the ear, so as to avoid injury to the superficial temporal artery. If the base of the pedicle is clamped early there will be no bleeding from the cut edge of the flap itself. In the occipital region the scalp can be turned down only as far as the superior curved line of the occipital bone, since below this it is firmly attached to muscle. Nevertheless, osteoplastic flaps can be turned down without detaching the scalp from the muscles. The author finally discusses, in greater detail, the technic employed in the turning down of the various osteoplastic flaps.

PETERSEN, Montreal.

ON A FORM OF PROGRESSIVE MUSCULAR DYSTROPHY NOT DESCRIBED IN THE LITERATURE. J. M. VILLACIAN, Rev. españ de med. y cirug., December, 1928.

Two cases are reported of primary myopathy of hereditary character in a brother and sister. The hereditary character of the disease is shown in the fact that the father, an uncle and an aunt of the patients died of the disease, which developed also in two sisters, one brother and one cousin. The disease begins between the fortieth and forty-fifth year, is of progressive character and ends fatally from ten to fifteen years after the onset of the symptoms. The latter are: localization of the atrophic segments in the proximal parts of the limbs; symmetrical character of the atrophy and similarity of posture and gait while standing, walking, climbing, descending and getting up in the two patients studied; exaggeration of the lumbar flexure and displacement of the scapulas; lack of idiomuscular contraction; abolition of tendon reflexes and of electrical reactions. Motor weakness and atrophy begin almost at the same time in the arms and legs. The muscles of the head, neck and tongue are not involved. At first there are painful cramps, and afterward a sensation of stiffness during sudden flexion of the limbs.

The male patient was found to be suffering from syphilis (positive Wassermann reaction of the blood and other clinical symptoms). His sister probably suffered from the same disease, judging from certain symptoms observed, but serologic tests were not carried out. The author does not express definite opinions on the causal relationship of syphilis and the muscular dystrophy in the cases studied. No symptoms of endocrine disturbances were noticed, and opotherapic treatment failed to produce beneficial results.

NONIDEZ, New York.

SENILE CATARACT, ITS CAUSES AND NONOPERATIVE TREATMENT. A. SIEGRIST, Ann. d'ocul. **165**:874 (Nov.) 1928.

The two main considerations are the etiology of senile cataract and the possibility of preventing, arresting or producing regression without operation of the processes of opacification of the old crystalline lens. An excellent history of the pathogenesis of cataract since the time of Cornelius Celsus (50 B. C.) is given. Roemer attributes the opacities of the lens to cellular autointoxication, produced by the senile changes in the organism. These cytotoxins are retained by the cells of the lens and thus produce cataracts.

Siegrist also takes up Salus' and Vogt's ideas which controvert the theory of Roemer. The author's theory of cataract is that of senile degeneration, which is manifest not alone in the lens, but also in the endocrine glands. He considers the question of Steinach's ligature of the vas deferens, and that of Veronoff, implantation of the testes, and concludes that the fountain of youth is not a myth, that old age with its symptoms is not inevitable because of the laws of heredity; on the contrary, a great many of the symptoms attributable to age can be lessened or completely abolished. The author attempts to treat senile cataract with extract of endocrine gland, or the genital gland, the thyroid and parathyroid playing the most important rôle. This extract is made by a German firm and is called euphakine. Thirty-two cases of supranuclear cataract were followed for from one and one-half to three years. All the changes in the lens remained stationary. In two thirds of the cases there was slight improvement. If treatment was

discontinued, vision diminished. He does not attempt to cure ripe cataract, but he thinks he can arrest its development and encourages other ophthalmologists to try his method.

BERENS, New York.

SOME LIMITATIONS OF THE MONRO-KELLIE HYPOTHESIS. LEWIS H. WEED, Arch. Surg. **18**:1049 (April) 1929.

Weed discusses some of the limitations of the Monro-Kellie hypothesis in the light of recent experimental work. As laid down by Monro, the hypothesis states in general that the brain is enclosed in a case of bone, and that within a rigid container, such as the cranium, the contents must at all times be of the same volume.

Weed estimated carefully the changes in cerebrospinal fluid pressure, intracranial, arterial and venous pressure, and general fluid pressure in a series of dogs shifted suddenly from the horizontal to the vertebral head down or tail down positions. As a result of these experiments, he thinks that the spinal dura must be in some measure distensible since it is not confined within an absolutely rigid container. This fact does not interfere to an important degree with the Monro-Kellie hypothesis, because the importance of this part of the central nervous system is relatively not so great as the cranial portion.

The Monro-Kellie doctrine, therefore, must be considered essentially correct in almost every physiologic way, though such consideration must always be subject to especial limitation. From the standpoint of intracranial physiology, as a basis for experimental or surgical procedures, the doctrine holds, and its importance is great in any clinical procedure.

GRANT, Philadelphia.

STUDIES ON X-RAY PICTURES OF THE CEREBRAL ARTERIES OF THE LIVING DOG. W. JACOBI, Arch. f. Psychiat. **86**:240 (Jan.) 1929.

The author has attempted to obtain x-ray pictures of the cerebral arteries by injection of chemicals into the carotid arteries of living dogs. For this purpose he experimented with three different substances: (1) bromide of strontium, (2) a 20 per cent solution of sodium iodide and (3) an organic iodine compound on a colloid base. These chemicals were injected in quantities of from 10 to 20 cc. The results are summarized as follows: (1) Ten dogs were utilized for these experiments, three of them receiving injections of bromide of strontium, two sodium iodide and five an organic iodine compound. (2) Two animals died immediately after the injection (one of bromide of strontium and one of an organic iodine compound).

The vessels were best demonstrated by the injections of bromide of strontium and an organic iodine compound, but the sodium iodide was apparently less dangerous than the other two. The vessels thus injected could be followed out to some of the smallest peripheral branches, and considering the fact that the vessels here are smaller than the ones in the human beings, one would expect much better results in the latter. The author thinks that such attempts should be followed up further, and when a definitely harmless substance is found it may lead to discoveries of methods that would be useful in diagnostic procedures.

MALAMUD, Foxborough, Mass.

IPSOLATERAL EDEMA AND CONTRALATERAL JAUNDICE ASSOCIATED WITH HEMIPLEGIA AND CARDIAC DECOMPENSATION. IRVINE H. PAGE, Am. J. M. Sc. **172**:273 (Feb.) 1929.

Two cases of hemiplegia of embolic origin with ipsolateral edema and contralateral jaundice are reported. The edema, occurring on the paralyzed side, is explained as being due to a vasomotor paralysis or instability and this suggests a direct control of cell permeability by the nervous system, the transudation of fluid not being due to dilatation of the capillaries but to a change in permeability of the cells. This condition is increased by local arterial hyperemia, which results

from vasomotor paralysis and causes an increased filtration pressure. Local anoxemia is suggested as one of the possible causative factors in the increased permeability of the cells.

There are two types of jaundice, the hemolytic, which gives a positive indirect van den Bergh reaction, and the obstructive, which gives both a direct and an indirect van den Bergh reaction. The jaundice in the two cases presented was of the second or obstructive type. The suggested reason for the lack of jaundice on the paralytic half of the body is that the turgor of the cells, due to the edema, may in some way hinder the entrance of the pigment.

WAGGONER, Philadelphia.

A HISTOLOGIC DESCRIPTION OF PIGMENT DISTRIBUTION IN THE EYES OF GUINEA-PIGS OF VARIOUS GENETIC TYPES. P. W. GREGORY, J. Morphol. **47**:227 (March 5) 1929.

A histologic study was made of the distribution of melanin pigment in the normal dark eye, brown eye, light and dark salmon eye, albino, pink eye, and pseudopink eye of the guinea-pig. The appearance of the density and location of pigment in the living eye gives an excellent indication of the actual density and distribution. All the genetic types studied reveal pigment in sections. The albino was found to contain the least amount of pigment, and certain types of the pseudopink eye, presumably those of the light salmon type, have only slightly more pigment than the albino. Certain pink-eyed animals have an appreciable amount of pigment in the deeper retinal layer in the region of the orbiculus ciliaris. The light and dark types of salmon eye reveal more pigment in the pupillary margin of the iris than in any other region. The deeper layer of the retinal epithelium contains slight amounts of pigment throughout. The difference between the pigmentation of the light and the dark salmon eye is quantitative. All animals which are not albino, pink eyed or salmon eyed have a large amount of pigment in the tissues of the eye. The wild type of dark eye contains the greatest amount of pigment in all regions. In this type the deeper layer of the retinal epithelium is the most deeply pigmented part, and in all types of eyes with reduced melanin, pigment persists in this layer even when it is absent from other regions. In eyes that have a reduced amount of pigment there is a decided tendency for the chromatophores to be located around the blood vessels. This tendency is outstanding in the iris and noticeable in the choroid. The genes that affect pigmentation in the eye have definite qualitative or quantitative effects on the production of melanin.

WYMAN, Boston.

EFFECT OF NONSPECIFIC PROTEIN THERAPY ON OCULAR CHANGES IN MULTIPLE SCLEROSIS: PRELIMINARY REPORT. G. W. HALL and R. C. GAMBLE, J. A. M. A. **92**:297 (Jan. 26) 1929.

No organic nervous disease is of such common interest to the ophthalmologist, otorhinologist and neurologist as multiple sclerosis. The authors believe that its early symptoms are not being detected sufficiently often, and one reason for this report is to stimulate the cooperation of the specialists named. The classic triad of symptoms appears late, and ocular signs and symptoms may appear and reappear months or even years earlier. Conservatism regarding operation on the posterior sinuses is recommended.

E. D. Davis presented statistics of seventy-six cases of retrobulbar neuritis in which syphilis was a cause in nine, infected teeth in seven, nasal suppuration in five and multiple sclerosis in fourteen.

That multiple sclerosis is due to an undetermined infective agent is now generally accepted. On this premise the authors base hope in their method of treatment, which consists in intravenous doses of typhoid and paratyphoid vaccine sufficiently large to produce a chill and rise in temperature following. Vaccine was given every other day for twelve doses. The visual fields were studied repeatedly. Some patients have received three courses with a rest period of from four to six weeks between courses. Of twenty-five patients treated, eleven are reported with the results of ophthalmologic examinations only.

The authors conclude that they cannot yet form definite conclusions as to the effect of this treatment on the visual changes. They think that there is general physical improvement, a fact already established in the literature. This method of treatment will, in their opinion, prove its real worth if it can be instituted before the development of the cardinal symptoms.

CHAMBERS, Syracuse, N. Y.

STUDY OF THE IRON REACTION IN THE BRAIN: II. INVESTIGATIONS OF PARETIC BRAINS. T. VON LEHOCZKY, Arch. f. Psychiat. **85**:229 (Sept.) 1928.

In this second communication, the author reports the results of investigations of iron reaction in paresis. In twenty-nine cases of clinically and microscopically diagnosed paresis, the iron reactions were as follows: Twenty-five cases showed diffusely distributed iron deposits, practically always in the vicinity of the vessels. This reaction was equally strong in the cortex and corpus striatum; it was weaker in the substantia nigra; in the thalamus, pallidum and red nucleus it was either weak or absent. In three of the other four cases the distribution was "atypical," i. e., present only in a few places, and did not conform to the localization in the other twenty-five. In one case the iron reaction was altogether negative. On the basis of these observations, therefore, it appears that although a certain type of iron reaction can be considered as characteristic of paresis, it is not always found. A positive iron reaction of the paretic type would speak strongly for the diagnosis of this disease, but a negative observation would not necessarily exclude this diagnosis.

Two types of iron can be described in paresis: (1) the perivascular iron which is found in the perivascular lymph spaces, in the adventitial cells or even in the form of free flakes, whereas none of it is found in the lymphocytes or plasma cells; (2) the microglial iron, which is found in the microglia, mostly in the vicinity of blood vessels. The author found no iron in any of the other ectodermal elements. The amount of iron does not necessarily correspond to the intensity of the inflammatory infiltration, a factor which is helpful in the diagnosis as is also the fact that none of the other forms of neurosyphilis show the paretic type of iron reaction. The author has found that treatments with malaria or milk injection have no influence on the amount of iron. He is of the opinion that the iron found in paresis is probably of hematogenous origin, and also that the microglia cells take up this type of iron probably because they possess a special affinity for it.

MALAMUD, Foxborough, Mass.

CALCIUM THERAPY IN ATOPY. Current Comment, J. A. M. A. **92**:317 (Jan. 26) 1929.

When a therapeutic procedure tends to become a medical fad, it should be subjected to critical scrutiny, not because of inefficacious methods but rather because too much dependence on any one form of treatment is liable to be at least detrimental to patients. Calcium therapy has attained a vogue that seems out of proportion to the demonstrable facts furnished by the clinic. The physiologic importance of calcium is disputed by none. But the tissues are continually bathed with a calcium-containing medium of fairly constant composition, and hypoglycemia is uncommon.

A number of anaphylactic or atonic conditions have been ascribed to a relative deficiency—presumably in circulating calcium—causing an imbalance with potassium and a consequent vagotonia with bronchospasm and asthma which would be expected to yield to calcium therapy.

Criep and McElroy have recently studied 167 cases of asthma, hay-fever, vasomotor rhinitis, urticaria and angioneurotic edema. They first established that 10 mg. of calcium per hundred cubic centimeters of blood is normal. They are convinced that there is no demonstrable calcium deficiency in atopic conditions. They aver that calcium therapy seems to produce no permanent increase in blood

calcium. They admit occasional objective improvement after the intravenous administration of calcium but believe that this influence is the result of the general depressing action of calcium on all tissues, especially the nervous system, as well as the result of the tendency of calcium to lessen tissue cell permeability and thus reduce transudations.

CHAMBERS, Syracuse, N. Y.

THE HEREDITARY TYPE OF ANGIONEUROTIC EDEMA. HAROLD F. DUNLAP and WILLIS S. LEMON, Am. J. M. Sc. **177**:259 (Feb.) 1929.

Angioneurotic edema is described as a condition of acute massive ephemeral swelling of the skin, mucous membrane or viscera, which recedes without leaving a residue. It shows a marked tendency to recurrence, especially in a previously involved area. The condition is chronic, lasting over many years, often in patients without demonstrable organic disease; each attack lasts from a few hours to days. It has been regarded as a form of urticaria by some authors, and many believe it to be the same type of disease.

The etiology is not known; temperature changes, anaphylaxis, toxins and autotoxins, infections, use of alcohol and chemical changes in the blood have all been described in association with angioneurotic edema, but the definite relationship of any of these to the condition has never been established. It has also been described in nervous disorders of both organic and functional types, but some believe that this form is not true angioneurotic edema. Heredity is an important factor, the condition being transmitted directly from generation to generation.

Four groups of cases have been described: In group 1—the most common form—the lesion is a large, pale, surface swelling, developing rapidly, lasting indefinitely and receding quickly. It does not pit on pressure. It is usually preceded by intense itching in the area involved. Groups 2 and 3 involve mucous membranes, usually the larynx, and are most dangerous because of the possible choking. Group 4 is the gastro-intestinal type, which may occur alone, with group 1 or alternate with it. Colic is the predominant symptom of this type. Groups 1 and 4 rarely cause death; groups 2 and 3 do so frequently.

In the cases reported in this paper, some showed definite changes in blood volume as studied by the authors.

WAGGONER, Philadelphia.

PRENATAL PREVENTION OF POTENTIAL HEMORRHAGIC DISEASE OF THE NEW-BORN: I. NEWTON KUGELMASS and JOHN E. TRITSCH, J. A. M. A. **92**:531 (Feb. 16) 1929.

True melena neonatorum is a distinct entity when gastro-intestinal hemorrhage and a progressively prolonged clotting time dominate the entire picture. In differential diagnosis one must consider the hemorrhagic diatheses of the new-born infant secondary to sepsis, thrombocytopenic purpura, congenital syphilis, congenital visceral anomalies and abdominal tumors. The blood clotting time in true melena is not conclusive for determining the hemorrhagic tendency of a new-born child. The important element is the quantitative determination of the clotting components of the blood, melena neonatorum giving a marked decrease in the prothrombin content of the infant's blood. Since the fetal blood is in equilibrium with the maternal blood, a study of the maternal blood in early pregnancy as to clotting components would offer a prediction of potential hemorrhagic disease developing in utero and thus offer a field for preventive prenatal therapy.

The authors present such a case in a woman who had five pregnancies; the first four ended in death from hemorrhagic disease in three new-born infants and possibly also in the fourth. The mother's blood at the second month of pregnancy showed poor clotting function and low prothrombin content, the characteristic feature of true melena as already mentioned. These clotting components may be altered by nutritional measures, and those used in this case are presented. The maternal blood became normal before the birth of the fifth child, who was a

normal nonbleeding infant. This case suggests the value of prenatal treatment in producing normal children. Further work on the subject is in progress.

CHAMBERS, Syracuse, N. Y.

TETANY AND TETANY PSYCHOSIS. E. FUENFGELD, Arch. f. Psychiat. **84**:363 (Aug.) 1928.

The author discusses the question of the occurrence of mental disturbances as symptoms of, or coincidental with, tetany. For a time the author has been using a special diet in the treatment for tetany. This is a meat-free diet with the addition of from 0.25 to 0.5 liters of milk and an especially prepared dried animal blood daily. This has proved beneficial in the treatment for tetany, and the author has investigated the effects of this diet on the mental disturbance. He first reports some cases in which the patients did not show any definite mental signs and in which the diet apparently helped materially in bringing about recovery. Then three cases of somewhat atypical circular psychosis are reported in which there were also definite signs pointing to tetany. The patients were treated in the same way as in the first cases with good results as far as the symptoms of tetany were concerned, but apparently without any effect on the psychosis itself. In another case in which mental symptoms occurred, which belonged to the type described by Kleist under the title of episodic twilight states, the patient also showed signs of tetanic diathesis. In this patient, too, the tetanic signs responded to the diet, but the psychotic phenomena were not affected.

The author concludes that the special diet is of great value in checking the symptoms of tetany, but that no such effect can be obtained on mental disturbances occurring in such persons, and therefore there seems to be no relation between tetanic diathesis and any type of mental disturbance.

MALAMUD, Foxborough, Mass.

CRITICAL REMARKS REGARDING THE PSYCHOGENESIS AND PSYCHOTHERAPY OF EPILEPSY. EMIL REDLICH, Nervenarzt **2**:1 (Jan. 15) 1928.

In this article the author reviews the question of the psychogenesis and psychotherapy of epilepsy. Many writers have attempted to explain epilepsy on a basis of psychic causes, but it is questionable if such a theory is tenable. There is little doubt that frequently hysterical factors are present in epileptic patients and that not uncommonly attacks are precipitated by emotional disturbances. The mere fact that a convulsive seizure or a petit mal attack may follow the hearing of music need not indicate that the underlying basis is psychogenic.

Redlich emphasizes the fact that it may be extremely difficult to distinguish between hysterical and epileptic seizures, and that much of the analysis that has proved successful may have been carried out in patients with hysteria rather than epilepsy. Bonhoeffer has used the term "reactive epilepsy" to distinguish those cases in which true epileptic attacks appeared to follow emotional disturbances. The psychoanalytic school, noteworthily Clark and Stekel, are convinced that many patients with epilepsy have been cured by psychoanalytic measures. It is, however, to be questioned whether these cures were permanent and if so, whether medicinal agents were employed to supplement the psychoanalytic treatment.

With all due consideration for the analytic school, Redlich is of the opinion that, even though psychoanalytic measures may be beneficial in the handling of epilepsy, certainly one cannot accept any such therapy for the entire group of epileptic disturbances.

MOERSCH, Rochester, Minn.

FACIAL DIPLEGIA. FRED P. CURRIER, Am. J. M. Sc. **175**:811 (June) 1928.

Two cases of facial diplegia are presented — one supposedly a polyneuritis or neuronitis with partial recovery, and one a case of myasthenia gravis with a clinical picture closely resembling that of the first case. The author presents a classifica-

tion which he considers applicable in either the unilateral or the bilateral type: (1) congenital defects—absence of the nucleus or of the nerve peripheral to the nucleus, or a defect of the bony canal through which the nerve passes; (2) infections—either at the site of the lesion or by extension; (3) toxic—(*a*) from infection elsewhere, and (*b*) from drugs, etc.; (4) trauma—(*a*) operative procedures, (*b*) puncture wounds, (*c*) skull fractures, (*d*) vascular accidents near the nucleus or the nerve, (*e*) injuries at birth and (*f*) pressure from tumors.

Multiple neuritis with facial diplegia is considered as being caused frequently by epidemic encephalitis or allied conditions. This possibility is considered in the first case presented although no postencephalitic manifestations have been noted. In the second case, there were several remissions, each apparently induced by, or associated with, the clearing up of some focus of infection.

WAGGONER, Philadelphia.

ENCEPHALOGRAPHY IN TUMORS OF THE POSTERIOR FOSSA. FRITZ EUGEN FLÜGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **115**:551 (July) 1928.

Tumors of the posterior fossa often give an indistinct clinical picture; hence, encephalography is of value. In addition to the ventricular dilatation which accompanies these lesions, Jüngling pointed out that there is another characteristic which consists of a shadow slighter on the side of the tumor than on the opposite side. This is due to a shortening of the posterior horn owing to pressure by the tumor from below. Air was introduced in Flügel's cases by means of ventricular puncture. Four views were taken: one anteroposterior, one posteroanterior and two lateral views. Flügel found in two cases that the posterior horn is compressed on the side of the tumor in the posterior fossa, and this compression is shown by a shortening of the posterior horn on that side.

ALPERS, Philadelphia.

VITAMIN B: ITS NATURE AND ITS WORKS. Editorial, J. A. M. A. **92**:562 (Feb. 16) 1929.

A brief history of vitamins is presented. Investigations since 1911 have shown that vitamin B is concerned with conditions other than beriberi. It has been shown to have growth-promoting qualities, and a certain fraction of the vitamin B complex has been shown to be concerned with the prevention of pellagra. Owing to the confusion now existing in nomenclature, Kruse and McCollum suggest that the term vitamin B should be applied to that fraction having antineuritic properties, while vitamin F could be applied to the antipellagrous fraction. The nature and effects of vitamins vary with conditions. The antineuritic properties of vitamin B are destroyed by a temperature of from 115 to 120 C. for from one to two hours. Ordinary cooking has little effect. This vitamin is acid resistant but alkali sensitive; it is little affected by ultraviolet rays and storage.

CHAMBERS, Syracuse, N. Y.

A TUMOR-LIKE NODULE IN THE LATERAL WALL OF THE SPINAL CORD IN A HUMAN EMBRYO OF 16.5 MILLIMETERS. ARTHUR BERGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **116**:687 (Oct.) 1928.

The embryo here reported showed, in addition to the nodule to be described, a reduplication of the central canal in the caudal portions of the spinal cord. Furthermore, there was a small cleft in the roof of the mesencephalon. Microscopic examination of the embryo showed at the level of the fifth lumbar segment a small epithelial nodule projecting into the central canal. This nodule extended over thirteen segments and measured 130 microns. It originated from the dorsal third of the lateral wall of the cord and from the zona ependymates. It was egg shaped. The epithelial cell proliferation arose from the zona ependymates.

ALPERS, Philadelphia.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 5, 1929

S. PHILIP GOODHART, M.D., *Vice-President, in the Chair*

PSYCHOLOGIC THERAPY IN DISSEMINATED SCLEROSIS, POSTENCEPHALITIS AND THE ANXIETY AND FEAR NEUROSES IN FEEBLEMINDEDNESS. DR. L. PIERCE CLARK.

In addition to chemical, toxic, endocrinic and metabolic studies in chronic nervous diseases, a steadily advancing research is being brought forward in relation to their psychologic physiology. Interest is not centered solely on physiobiologic disturbances of various functions (Cannon) or on the psychobiologic problems of the organism as a whole (Paton, Meyer), but many investigators are turning their attention to the mechanisms of the unconscious in which, according to Freud's metapsychology, the instincts may be at fault. The repressions and perversions of the instincts are therefore the main inquiry.

I believe that one will make better progress if one disregards for the time being the whole picture of the morbid syndrome of the organic nervous disorder and allows some other physician to take care of it as such. Or better still, it would be well for the patient to disregard the immediacy of neurologic treatment while psychoanalysis is in progress, for unless the cooperating physician has been analyzed himself, he is likely to take so much of the patient's transference that the latter cannot be analyzed while the physical therapy is in progress. The well known tendency is for the physician, whether he has been analyzed or not, to influence the patient unconsciously in the belief that his difficulties can be remedied by the specific therapy the physician applies. As most patients suffering from chronic nervous disorders frequently go months without active chemical or physical therapy, the intervening period may be employed advantageously for analytic therapy solely.

For the present, it must remain a moot question how much the peculiar morbid condition of the brain which invariably accompanies organic nervous disease influences the total disorder or is really a part of its pathogenesis. No one denies that the morbid clinical picture is distorted by the neurotic attitude the patient takes toward his condition. It varies in proportion as the functioning of the organism as a whole is requisitioned in living. Many have not been content to assume that the morbid condition of the brain in these patients is subsidiary or only a part of the symptomatic pathogenesis, but have analyzed the whole personality as though the patient had no actual physical disorder. It is as though one asked the patient to exclude for the time his concern in his distressing plight and invited him to analyze his whole personality or character neurosis, so that the specific disease may be flanked or rendered unnecessary in the light of a broader and deeper comprehension of his total living activities. Thus the organic disease may be freed or its hold on the bodily functions greatly lessened. To the patient it may sound like bitter irony to be asked by the analyst to accept a larger concern that will embrace the total libido rather than the specific defect which presses for riddance. As in essential epilepsy, in drug addiction, dypsomania and other constitutional disorders, one does not make progress in treatment until the patient can be induced to give attention to the underlying unconscious motivations. The all too dominant nosologic treatment for organic diseases of the nervous system may be responsible for the present dilemma.

To continue to think of the patient in terms of his neurologic symptoms and interpret his analytic material in such a light not only curtails the possibility of

a riddance of his actual physical symptoms but may prevent any deep thoroughgoing analysis. In other words, at the outset both the patient and the analyst must look on the analytic situation in the terms of freudian psychoanalysis, and let the outcome be as it may. The tendency to keep a neurologic view in sight must be considered resistance on the part of the analyst as well as of the patient.

The first requisite for the analyst, if he is also a neurologist, is to rid himself, by his own analysis, of this tendency toward resistance. This, of course, is difficult in the extreme, as it embraces the whole narcissistic formation of the character. Unfortunate as this state of affairs is at present, crippling as it will prove to be to the real advance of pure psychoanalysis in the organic field, it will have to be borne and guarded against until analytic therapy is as fully recognized as a proper procedure in these patients as it is acknowledged to be in transference neuroses.

Shall all these matters of technic be worked out esoterically in purely psychoanalytic societies, or shall they be brought out for perhaps less keen technical discussion in the field of the first detection of these nervous disorders? In other words, these patients are first seen by neurologists, and the latter are entitled to have an opportunity to discuss the plan of analytic research and therapy which one proposes to put into effect in relation to organic nervous disease. From time to time, psychoanalysts hope to place their researches before this society and report their progress.

The first case which I shall set forth briefly will be the results of a short period of analysis in a man with disseminated sclerosis of nine years' duration who made a partial recovery. The second is that of a conduct disorder in a girl affected with postencephalitic disease for four years who, after several months of modified analysis, apparently made a complete recovery. The third is that of a boy now aged 17, with mental arrest, in whom analysis brought out a deep fear neurosis. While the neurosis and conduct disorders were in the process of being removed, the intelligence quotient apparently advanced from 7 years to 9 plus in the space of three years; the boy is making better social adaptations and is attending a public school where he is taking special studies. Last fall, he passed a test which made him eligible to enter the first year of high school. The teachers recognize that he is a difficult problem and have made allowances for his obvious handicaps. The algebra teacher believed that he might be able to gain a passing mark this year, but doubted whether he had sufficient foundation to attempt higher work in mathematics. The German teacher was inclined to believe that he would make the present grade. The English teacher considered that his weak point was in written work; his oral work in this class was excellent. She said, "When it comes to discussions he can talk by the hour, and gives a very good account of current topics." In typewriting, he reached a passing mark of 84 per cent.

The patient with disseminated sclerosis had a typical case, and though he was given none of the usual rest, care and tonic upbuilding which had been instituted on previous occasions with no improvement, after several months' analysis not only did he show marked improvement in general health but the knee jerks were diminished, ankle clonus was absent, the intention tremor nearly disappeared, and the distressing diplopia vanished to the point where he could almost entirely discard glasses. I am not unmindful of the fact that fully as dramatic results have been brought about by suggestion or even complete rest in bed and tonics, but that such a result is possible solely by psychoanalytic treatment is noteworthy.

Under analysis, the patient's business life was found to be of the nature of a compulsion. His whole trend of interest had been to live in the country and lead a farmer's existence, the occupation of his people. He had been induced to follow a business career by his father and uncle. His infantile fear and dependence were marked. He always clung to the bars of the bed at night for safety and security, until finally the paint was worn off the bedposts. His youth was clouded by imaginary fears of robbers, wild animals, gypsies and kidnappers. All sorts of exorcisms, as protections against these fears, were secretly practiced, and all symbolized mother dependence. His father was feared, respected and hated. In

his day and night dreams, he was engaged in ingenious flights from his fearful predicaments. His passion for the country was found to be neurotic and romantic; his farm, a part of his possessions, was actually neglected and managed by others. He permitted his relatives to interrupt his treatment in spite of the remarkable benefit he obtained in the short period of analysis.

In brief, psychoanalysts will easily recognize the well known transference fear neurosis with its infantile dependence, and the masochistic mechanisms which seemingly induced the severe organismic tension; this tension seemingly aggravated, if it did not provoke, the organic spinal disorder. The patient is now back at work and is apparently in fairly good health.

The occurrence of conduct disorders in the wake of encephalitis in children and adolescents is continually of such distressing and despairing report that any form of therapy that promises any degree of enduring relief is doubly welcome. Several years ago, I formulated a hypothesis for the narcissistic neurosis of this type of conduct disorder. The main postulate was that the encephalitic process, whatever its site or range, invariably injured the ego organ, the brain, and that, proportionate to the site and depth of the wounding lesion, libido was there impounded to aid in healing the lesion, and failing this, libido was continually bound up in these injured structures and caused a deep regression of behavior and emotional expression. My remedy at that time as now was to resort to psychoanalysis with narcissistic countertransference. By thus gently penetrating the narcissistic formations about the ego, one assists the patient to place reliance on that part of the narcissism that was most nearly adjustable to adaptive reality and thus assists the patient successfully to repress the strong egoistic concern and activity and allows the libidinal complement of the ego, the narcissism, to work out its more natural cathexis in everyday life. At that time, I did not think that there was any appreciable amount of objective transference of libido with which one might conduct any ordinary psychoanalysis comparable to that in a simple neurosis. Since then I have found out differently, and I now hold that the slight evidence of the presence of even a small objective transference is sufficient to use for ordinary analysis. The presence of the fear element, or the evidence of some degree of anxiety, gives a clue to the presence of this displaceable affect by which one can reach these patients. The following case will illustrate this point:

A girl, aged 17, came under treatment early in May, 1928. Her most marked symptoms were a restless pacing up and down, accompanied by puffing and gasping for breath, reeling dizzily and sometimes falling unless caught. She was pale and delicate, and became fatigued on slight exertion. She slept poorly and ate her meals in bed. She demanded constant attention and expected nurses and attendants to anticipate her slightest wants.

When Dr. Meagher saw this girl in 1924, he described the case as a mild attack of encephalitis in which involvement of the third nerve and lethargy were the prominent features. When she began to exhibit psychopathic reactions after this attack, he referred her to Dr. Jelliffe, who described the respiratory attacks as follows: "She would commence to breathe harder and harder and make sounds and noises; in some of the attacks she would get up on tip-toe, go in menagerie-like motions about the room, eyes and head to the left in a tonic cramplike position with heavy breathing, and often saying and grunting, 'Don't touch me, don't touch me.'"

After a few days, analysis was attempted. The same restlessness accompanied by puffing and gasping characterized the sessions. For the first few weeks the sessions were short, as she quickly tired and would start to pace up and down and go into a respiratory attack. The tantrum phase became so marked as to interfere with the analysis. She became violent toward her nurses, refused to allow them to sleep, screamed at the top of her lungs at any hour of the night, broke windows, slammed doors, tore up her own possessions, in short, stopped at nothing in venting her temper. The tempers were always worse at night, and were at their height from early morning till 9 or 10 o'clock. She fell down a

great deal during the respiratory attacks, suffering bruises from head to foot yet protesting angrily and threatening violence if anyone tried to help her.

From September till her departure near the end of November, she made great improvement in these behavior reactions. She formed a fairly strong transference. Her physical symptoms, such as the respiratory attacks and sleeplessness, cleared up almost entirely. She now sleeps without a sedative, eats at regular hours and, during the last month of her stay, mingled with the group in all their social activities.

The analysis, which was only properly psychoanalytic for two months, showed an extreme emotional infantilism and its sequential narcissism. The auto-eroticism was marked; yet a fairly stable transference continued.

It is necessary for me to report here, as in the preceding case, that perhaps as strikingly dramatic a recovery from the neurotic syndrome was obtained by a treatment that was almost wholly psychoanalytic after all other forms of treatment had failed, and at the introduction of psychoanalysis the change was immediate. In this patient, pubescence had begun several months prior to the encephalitic process; the most distressing regressions in conduct occurred, and at the first induction of psychoanalysis the completion of an arrested pubescence was once more undertaken. The patient began to notice boys, assumed flapper habits and attitudes and the auto-erotic needs were once more in evidence. She became more socialized, quieter and gained in weight. Was she about ready to undergo this spontaneous recovery or did analysis merely make the process more easy and rapid? Or is the analysis in such cases more to be prized than some would concede? There is no evidence of there being any purely endocrinic imbalance. I feel certain that only the reaction in further cases can determine the exact rôle of psychoanalysis in such encephalitic patients. Finally, the so-called specific organic syndromes of respiratory attacks which are now absent are shown perhaps to be not a little conditioned on psychogenic incitation, and are not so hopeless of alteration as many suppose. Several other cases of the striatal types show similar improvement in the progressive syndrome as well as in the psychotic pictures of depressions and sexual perversions. They will be reported at some future time when I am able more accurately to evaluate the different factors in each case.

My last case is presented to show that in the immense repository of mental arrest a few patients often exist who do not owe their mental defect to a congenital or an acquired brain defect; they may possess an intensive fear neurosis that so overlies the real picture that the patient not only may appear feebleminded but may possess an intelligence quotient that places him in the class of the imbecile.

This boy, whom I am presenting here had an intelligence quotient of 7 years when he came to me four years ago, and now shows an intelligence quotient of 9 plus. He is an officer in his Boy Scout troop and is an expert designer and weaver on the loom. His general deportment and conduct have undergone the greatest change. His case was partially detailed two years ago in a published monograph and will be presented again in a later publication. He is now 17 years years of age and came under care as a feebleminded patient with conduct disorders and as one who could not be taught in the ordinary way either in public or in private schools. The following portraiture of the boy in his behavior reactions will present the salient characteristics which I undertook to analyze.

On first acquaintance, he gave the appearance of great shyness. With side-long glances he answered questions shortly and defensively, giving the impression that his questioner might be a possible critic. He seemed satisfied with what he was and what he knew. He appeared firmly resistant. Once he was shown definite friendliness and approval without demands on him, he quickly attached himself to the new acquaintance. He formed immediate crushes and eagerly looked for opportunities to do favors, run errands and perform helpful service. He would linger around his new friend, displaying his knowledge of adult subjects, boasting quite frankly of his father or of his friends, telling stories of unusual experiences —all with the firm insistence and dogged resistance to correction that would be expected in one who was sure of himself. Many of his statements defied belief,

but despite obvious absurdities and inconsistencies he continued to stand firm. When confronted with proof or obvious logic he still maintained that he was right, clutching frantically at his last straw—that things in his home town were different, or, with voice rising higher and higher, that his story was true no matter what was brought to bear against it. Tantrums were not unusual when forcible action was taken to carry out discipline or authority. In these, after his first withdrawal and hardness, he would viciously kick and scratch to prevent his defeat. Only friendly assurances, together with constant inspection, could induce him to take the ordinary steps for cleanliness, and frequent tantrums arose in this connection. His boasting, display of superior knowledge and lack of interest in physical games made it difficult for him to get along well with boys of his own age. He preferred to be with older people, excusing his failure to mix with boys on the ground that his physician told him that sports would be dangerous on account of his eyes (a double squint). He liked to study, to read and to discuss adult subjects.

One may easily recognize here what was found on more precise analysis: the simple type of a fear neurosis and a strong tendency to masochistic reaction. The narcissistic element is still marked. He has been under analysis for three years.

In conclusion, I wish to state that the first case may encourage neurologists in the future to look for the psychogenic factor in disseminated disease more carefully, or at least to recognize that the almost classic disseminated sclerosis may have a psychopathologic condition that can be utilized for the betterment of these chronic invalids, and perhaps, in the earliest beginnings, that the lesion may even be brought to a regressive arrest.

Regarding the second case, I hope that careful scrutiny may show more of such patients with encephalitis and conduct disorders who may signally improve, if not be cured, in the same way.

In the third type of case, that of a fear neurosis masquerading under feeble-mindedness, the removal of the neurosis may permit a better mental development or a possible escape from the mental defect entirely.

DISCUSSION

DR. H. W. POTTER: I do not feel competent to say anything about the first two cases. I admire Dr. Clark's fearlessness in his attack on these cases, but there are certain things which I think one ought to consider carefully in relation to his last case. First, there is considerable doubt in my mind whether this boy can properly be classified as a mental defective. To classify a person as mentally deficient, it is necessary to prove three things: (1) that he is socially ineffective; (2) that this social ineffectiveness is due to a deficient or defective intelligence, not to emotional complexes or things of that nature, and (3) that the defective or deficient intelligence is of the nature of an arrest or a lack of potentiality for complete development. I would be interested in knowing this boy's early history. Did he show retardation in general development at the ages of 1, 2 or 3 years? Another thing is that although this boy was presumed to be congenitally defective, mental deficiency is not merely a defective state of the brain or of the central nervous system; it is a general biologic inferiority, and one ought to find evidence of inferiority in other departments of the organism.

Another point is the fallacy of the intelligence quotient as a criterion for diagnosis. Any child who is emotionally disturbed, who is suffering from a fear neurosis, can give a low rating on nearly any one of the formal psychometric tests. Dr. Clark said that this boy's last mental age was 9 plus. I presumed that 9 plus means somewhere between 9 and 10; yet, on the other hand, I assume from what Dr. Clark said that he is doing some of the work of the first year of high school. That is impossible. No one with a mental age of 9 can do the work of the first year of high school. Such patients are fortunate if they are able to do fourth grade work; so it seems to me that there is some indication that the mental age as determined by psychometric tests does not indicate this boy's abilities or where he really ranks as to intelligence.

One other consideration is in reference to the increase in the intelligence quotient. I do not know why it happens, but nevertheless it does happen. I do not know whether it is because of some obscure psychoanalytic process that has been applied unconsciously by people in charge of the cases, but I have seen children who, shortly following puberty showed rather unusual gains in the intelligence quotient. For instance, I recall a boy who had a mental age of 8, and an intelligence quotient of 50 up to the age of 16. At that age he entered puberty, which was rather delayed, and by the age of 18 he had an intelligence quotient of 85. The same thing has happened in other cases, wholly without explanation.

DR. SMITH ELY JELLIFFE: I feel somewhat reluctant to discuss the first two cases of Dr. Clark's, chiefly because to do so adequately and constructively one would have to spend so much time. Of necessity, Dr. Clark has presented thumbnail sketches only. One must do Dr. Clark justice by assuming that, behind these thumbnail sketches, he knows about multiple sclerosis, about encephalitis and about feeblemindedness. He has been at it for thirty years, in constant touch with patients, and I think that he is thoroughly well grounded when it comes to a question of whether it is or is not this or that in the ordinary nosologic scheme of things. Two attitudes that are particularly difficult to meet in any discussion of psychoanalytic principles are to be found. Because of that, I am always reluctant to discuss papers on so complex a subject as psychoanalytic therapy. One of them is sophistication, and the other is fatigue. I listen to so many people who are so sophisticated. They know so many things that are not so that one cannot get anything into their heads. Charcot remarked many years ago, when Duchenne described his newly reported muscular dystrophy, "Why is it that something as plain as the nose on our faces, and that has been all around us for a thousand years, we suddenly wake up to and find it. Then, further, for twenty years, we try to tell others about it and they do not see it; and then all of a sudden they shift their point of view, and it is all so evident?" Thus for sophistication. The other element is fatigue. People are so lazy that they will not make the effort to allow ideas to enter into their brains. I have suffered for many years in meeting these two attitudes. Perhaps the condition Dr. Clark described is not multiple sclerosis, or encephalitis, or feeblemindedness; as for the second element, that of fatigue, it takes too much concentration to listen to new ideas, because to be able to reverse one's thought is extremely difficult. The point of view here brought forward needs to be emphasized. I, myself, am glad that Dr. Clark emphasized it again, because some of you will recall that at least twelve years ago I said something about the psychogenic component in multiple sclerosis, and four years ago I presented some material on the psychologic situation as it is found in encephalitis particularly in cases of encephalitis with respiratory complications.

In a modern setting of Plato's celebrated lines in his Charmides, about the necessity for treating the "soul" if one would treat the "body," I quote from Whitehead's "Science in the Modern World" (p. 113), which it strikes me might be of particular value in the discussion. He writes that "the concrete enduring entities are organisms, so that the plan of the whole influences the very characters of the various subordinate organisms which enter into it. In the case of an animal, the mental states enter into the plan of the total organism, and thus modify the plans of the successive subordinate organisms (that is, the organs), until the ultimate smallest organisms, such as electrons, are reached. Thus an electron within a living body is different from an electron outside of it by reason of the plan of the body. The electron blindly runs, either within or without the body, but it runs within the body in accordance with its character, that is, in accordance with the general plan of the body, and this plan includes the mental states." It seems to me that this is the crux of the argument which one has to meet, namely, that there is an electron within the body, taking part in the chemistry of the body, which runs according to the mental state; the purpose of the individual as a living organism determines how all the rest of the organs should be run. No one doubts, as Dr. Clark started his introduction by saying, that toxic elements

may come in as interfering with the goal toward which the whole plan has to adjust itself. Mechanical elements may enter in, but the whole plan of the organism is striving to reach its goal in accordance with patterns which have been in the formula for a billion years. One gets nowhere (I have said this fifty times) by studying the changes in the bodily chemistry as interpretative of causation, as, for instance, a study of the chemistry of the epileptic patient. One does not get real causes, one gets results. Such investigations are interesting and valuable as indicating the degree of change that the elementary bodily constituents have undergone by reason of the disturbance in the organism as a whole. It has reached such and such a stage with reference to its various physical and chemical properties in the epileptic patient or other sick person, encephalitic or not, because of the difficulties in the gradual change of the organism as a whole in its plan as a whole.

A great deal is to be said concerning the patient, concrete work in individual cases, in which hour after hour, day after day, month after month, year after year, attempts are made to get at some of these thwartings whereby the instinctual goal has been held up by a variety of situations. No one doubts that the spirochete entering into the organism and giving rise to paresis introduces a type of conflict within the human body which the plan as a whole is unable to handle. Thus the distorted situations which go on and receive the name paresis are inevitable and cannot be met by any readjustment of the plan as a whole, namely, by adjusting the mental system. The conflict of the energy system of the spirochete, or other energy systems, as in encephalitis, with the bodily energy system may produce such distorted compromises that one cannot do anything with them, but it is always worth while trying, because one never knows whether the line has been passed from a reversible to a nonreversible somatic situation. If a nonreversible situation is reached, from either the chemical or the microscopic point of view, then one feels that one cannot do much with what has already happened. One can get an enormous amount of information about it, however, by psychoanalytic study. Thus, for instance, I have studied half a dozen cases of multiple sclerosis for the last ten years; I always give the patients a definite statement before beginning just what I expect to do: I tell them that the situation is a purely research one, and that there is no promise of a cure. I repeat that I am trying an investigation which may reveal some of the dynamics of the situation. If the patient can cooperate one may arrive at something which may be of benefit to him in forestalling or preventing further developments along the usual line of the cases of multiple sclerosis. I have never cured a patient with multiple sclerosis. I have never attempted it. I have not seen one early enough in the disorder to alter a situation such as the Babinski reflex, for instance, into a reversible situation. This reflex is more or less an indication of a nonreversible situation; yet it may not be, as it is present in an epileptic attack, only later to disappear. I would not expect to get rid of the spasticity which is an accompaniment of that situation, but I have reason to believe that it might not progress. I know and Dr. Clark knows that many patients with multiple sclerosis (idiopathic, Müller) have regressions, just as patients with paresis have regressions, and that some patients with multiple sclerosis have more or less permanent regressions of the symptoms and make an apparently good recovery; however, this is aside from the issue. We here are interested merely in determining what the mental states have to do with the whole situation.

The case of the encephalitic patient whom Dr. Clark described is extremely fascinating to me because I have seen her on and off for three years. I saw her with Dr. Meagher, who referred her to me. She was then a little devil as well as a saint. I have dodged ash trays and other implements that she threw around in my office whenever her mother simply wrinkled up her eyebrows in mild reproach. She was so exquisitely sensitized to the slightest thought of what may be called hostility on the part of the environment that she was even affected by the lifting of an eyebrow or the closing of a fist. The mother, a charming person, was incredibly stupid from the standpoint of this young instinctual person. There was a constant fight. Dr. Clark may think that psychoanalysis cured her. I give him all the

credit he wishes, but if he knew the work I put on the mother he might give a slightly different interpretation. I doubt whether he would, however, and we can shake hands on the situation by saying that it was more or less the psychoanalytic knowledge on the part of the mother that helped the patient. The child first went to a sanitarium where there were a great many feebleminded boys. One of these boys got to monkeying around with her. She then started this menagerie "don't touch me" activity. Up to that time, she had not had any respiratory difficulties. She went through these menagerie movements, and she would grunt "don't touch me," which meant "don't touch my genitals," "don't masturbate me." It was quite plain just what "don't touch me" meant. She then went to Dr. Jacoby's sanitarium and led them a merry life there. She was still very sick, however, when she went to Stamford. Certain things happened there which brought out other components of consciousness. Thus, from the analytic understanding (there was no psychoanalysis by any "method") and with the analytic wisdom gained by the mother, she no longer struggled to keep this masturbatory situation from coming into consciousness with fear and horror. She accepted it. Then she fell in "love," and that was the beginning of her real cure. She fell in love, paradoxically enough, with at least two persons in the sanitarium. The transference was interesting. She had a fine, religious (superego) transference on one of the men teachers; on the other hand, there was a low, base, vile situation with somebody else in the environment. There the two situations, struggled for conscious mastery. Between the two, the whole material, plus the analytic interpretation, plus the knowledge of the environment, slowly came into the field of conscious control, and she was able to accept it all without guilt. I am not prepared to say that this is the full explanation of the case. I believe, however, because I have worked with some cases of respiratory encephalitis with respiratory complications now for four or five years with good results, that most of them show a striking course. At least 15 or 30 per cent of the patients get well spontaneously (see the figures of Ziegler, Critchley, Cook, Stern and others). Whatever "spontaneously getting well" means, nobody knows. There is really no such thing as spontaneously getting well. There are always a group of factors in the environment as well as internal ones which are of significance in the interpretation of results.

This second case illustrates the value of concrete, close work; whether it is modified psychoanalysis or straight psychoanalysis is more or less immaterial. It is the concrete, close work — patient, continuous, intensive, and intelligent — that counts.

DR. S. P. GOODHART: Dr. Clark has requested response to several pertinent questions, and has put them to us as organic neurologists. I should say emphatically that the question as to therapy, including the advisability of utilizing psychoanalysis, should be brought before a society of organic neurologists. We admit the inadequacy of our therapy and hence are only too willing to utilize any means for meeting the problems of organic disease. I should like to know whether Dr. Clark thinks that all organic cases have some etiologic factor of psychogenic origin and hence are influenced by psychoanalysis. He speaks of the relief of tension in his case of multiple sclerosis. That appears to be a corollary of what is implied when he speaks of the psychogenic influence on organic disease; while I do not expect to have a clear, lucid explanation of what is meant, I am sure an elucidation of his idea of what he expresses as the release of tension and its influence on the pathologic condition in such diseases as multiple sclerosis and encephalitis would be appreciated. There is much to warrant the belief that there is a relationship between the emotions, the psyche itself and the disturbance of motility of organic origin. That is especially demonstrated in encephalitis in which in the early period of the disease, especially in those cases showing mania or hypomania, there is almost invariably a hyperkinesis; this is more true in the psychosis, especially the manic-depressive form. Hypokinesis and psychic depression and hyperkinesis and mania are grouped together. In encephalitis, indeed, the influence of pathologic changes in motor centers on psychic activities may explain the apparent

psychic retardation in the chronic inflammatory disease. These facts would tend to point to a relationship between the psyche and striatal pathologic changes. In other words, the apparent slowness of intellectual response in postencephalitis of the parkinsonian type may be due to a lack of associated response, as a part of normal accompaniment of thought expression. Psychoanalysis as a therapeutic measure is certainly not indicated in every case of organic nervous disease of the group of which Dr. Clark has spoken, and I am still unconvinced as to just how far the organic pathologic condition was directly or indirectly influenced by the psychoanalytic element of treatment.

DR. CLARK: Concerning Dr. Potter's criteria for mental defect, these were continuously noted in this boy from earliest childhood. He has been in many children's and neurologic clinics. His intelligence quotient was taken repeatedly by different experts, and all tallied in the main. Up to two years ago, no one doubted that the enfeebled mentality was permanent. There was nothing wanting in the picture of mental defect, and the added phobia was considered a negligible symptom. It may be that the endocrine system, awakened by a delayed and incomplete puberty, had something to do with the resultant improvement, but the latter was not in evidence until analysis had relieved the inner tension. Everyone knows that the intelligence quotient is not determinative of permanent defect in every case, but in most cases it is so largely inborn that one should hesitate before stating that the intelligence quotient has increased in any given case. It is well known that mental defectives may make great advancement in social and industrial adaptability while the intelligence quotient remains unaltered. The fear neurosis in this case was supposed to be only a part of the defense mechanism and was not looked on as the chief crippling factor to the whole mental life. When the neurosis was reduced in part, environmental stimuli could then influence the development. Many psychiatrists and psychoanalysts have seen the case in its process of continued development, and while it is unusual in type, I believe that many institutions have similar cases; a recognition of them would help relieve the otherwise gloomy outlook for these patients in whom the neurosis is masked as feeblemindedness. This work is a contribution to a more hopeful outlook in psychasthenics and in organic nervous disease. In both fields, betterments in prognosis and treatment are sorely needed. In the organic or constitutional field one cannot say which cases are favorable for analysis until analysis has been tried out. This much is known: analysis at the earliest time possible is the prerequisite for success so that the organic syndrome may be recalled to vital living in the psyche and refashioned for successful sublimation. Continued and painstaking trial without prejudice should be our guide. In all these constitutional disorders the analytic therapy takes time, much longer than the transference neurosis. Not only is it necessary to penetrate more deeply into the psychic formation of neural and bodily patterns, but the way to this end is beset with the greatest conscious and unconscious resistances. These patients continually rationalize their obvious organic disease, and one must spend a great deal of time in displacing the affect from these to the actual character defect of the total personality. Practically speaking, three or four years will be necessary for analysis in an early case of disseminated sclerosis. Perhaps in time one may learn short cuts or at least learn to diagnose such cases earlier, and then the task may meet with greater success. Perhaps endowment funds and the employment of many lay analysts will help in this arduous task. At present the lack of a constructive plan of attack not only has lowered the hopes for recovery of such invalids, but has debased all those who are consigned to their care in the belief that there is nothing further to be done once the diagnosis has been made.

STUDIES IN CHRONAXIA WITH A REPORT OF THIRTY CASES IN CHILDREN. DR. DAVID WECHSLER and DR. ROWLAND S. FREEMAN, JR.

This article appeared in full in the September issue of the ARCHIVES, p. 558.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 21, 1929

LOYAL DAVIS, M.D., *President, in the Chair*

SEROUS SPINAL MENINGITIS (CIRCUMSCRIBED): A REPORT OF TWO CASES. DR. GEORGE B. HASSIN and (by invitation) DR. EDMUND ANDREWS.

This paper will be published in full in a later issue of the ARCHIVES.

DISCUSSION

DR. PETER BASSOE: Pain is not a common feature in these cases, but one of the first cases that I saw was that of a young married woman whose only symptom was excruciating pain, practically limited to the area of the twelfth dorsal root on the left and brought on by movement. She was terrified by the pain. Dean Lewis did a laminectomy, which disclosed a typical circumscribed serous meningitis. In addition to incising the cystic meninges, he cut the twelfth dorsal root. It has been fifteen years since the operation. I have heard from the patient, and she has remained well. In watching laminectomies, it has struck me that sometimes one sees what appears to be an absolutely typical circumscribed arachnoiditis, so typical that it seems unnecessary to look further, but on going a little further down a tumor is encountered. It impresses me that the appearance is similar to what may be seen above a tumor, so that there is reason to be cautious about exploring further down.

DR. MEYER SOLOMON: Stookey has mentioned as a rather characteristic thing that in these cases he finds no increase of protein in the spinal fluid, while there may or may not be a spinal block; in the cases reported by Dr. Andrews there was no evidence of subarachnoid block.

DR. A. B. YUDELSON: Were microscopic changes found in the dura or the arachnoid in the first case? There is a boy in the Cook County Hospital who gives a history of having risen early in the morning about two months ago, with sudden paralysis of the left upper extremity. There is now a mild atrophy, with no sensory changes on the paralyzed side, but with anesthesia and analgesia from the level of the fifth cervical downward on the opposite side, and increased tendon reflexes on the normal side. There is no spinal fluid block. We suspect a condition of localized, circumscribed arachnoiditis in the cervical cord on the left, beginning at the fifth cervical, as in the first case reported by Dr. Andrews. There is no pain on the affected side.

DR. PERCIVAL BAILEY: In favor of Dr. Andrews' hypothesis that circulatory changes are responsible for some of the changes in tumors of the cord is the fact that many of the symptoms cannot be explained by the tumor itself. In tumors at the second and third cervical level, it is well known that atrophy of the small muscles of the hand may occur which may be so pronounced as to mislead one as to the localizing diagnosis. This atrophy must be due to circulatory or other disturbances in the cord below this lesion, such as the result of blocking of the spinal fluid or what not.

DR. EDMUND ANDREWS: Answering Dr. Bassoe's suggestion that this might have been due to an overlooked tumor below, our experience is that tumor is usually overlooked above this, but in that case one would not expect the patient to get well. I have always extended the incision as long as I could feel anything abnormal in either direction. I found normal arachnoid in both directions. Tumors usually cause blocking, and in this case there was no blocking. The only specimen I could get from the pathologist was a tiny shred of adhesions, which showed nothing.

Dr. Bailey spoke of circulatory disturbance. I do not know about the blood, but in Dr. Hassin's laboratory some work has been done on lymph, and I think it is as likely to be that as anything. We have injected air in several cases, but in none was there any evidence of blocking nor was there any change in symptoms following the injection. The fluid has ordinarily been under normal pressure, and there has been no block in any case.

PHYSIOLOGIC EFFECTS OF THORACIC AND OF LUMBAR SYMPATHETIC GANGLIONECTOMY OR SECTION OF THE TRUNK. GEORGE E. BROWN and ALFRED W. ADSON.

This article appeared in full in the August issue of the ARCHIVES, page 322.

DISCUSSION

DR. LEWIS J. POLLOCK: In Dr. Brown's opinion, are the arterioles and the capillaries affected alike by sympathectomy? Does he believe that the vasodilatation is the result of removal of the constrictor fibers alone? If not, has he in view something else to explain it?

DR. A. B. YUDELSON: Was herpes zoster observed?

DR. PERCIVAL BAILEY: Was the pilomotor reflex present, and did this disturbance correspond in area to areas of disturbance of sweating.

DR. D. M. OLKON: Were there any hemorrhages around the right-angle capillaries in your cases of thrombo-angiitis obliterans or in the cases of Raynaud's disease in your series?

DR. LOYAL DAVIS: The clinical results which Dr. Kanavel and I have obtained are in complete accord with those of Dr. Brown, particularly those in the lower extremities. I have no doubt that the reason the results were not so complete in the upper extremities is that we did not remove the second thoracic ganglion.

DR. GEORGE E. BROWN: Dr. Pollock's question is interesting, but an adequate explanation is not at hand. We have observed that following operation there is dilatation of the smaller arterioles, as shown by the changes in surface temperature, while the capillaries, as examined microscopically, become narrower in the cases of Raynaud's disease. In this disease, the tone of the capillaries of the skin is diminished and the capillaries are dilated. We have observed in one case of Raynaud's disease of long duration that the usual dilator effects occurred in the arterioles, but that the capillary tone did not improve to the degree expected; the hands would become red when dependent and assume a normal color at the heart level. These opposite effects in the arterioles and capillaries are probably due to the elimination of the vasomotor effects in the former. The narrowing of the capillaries seems to be related to the acceleration of the capillary flow with improvement in the oxygenation of the capillary blood and a diminution of metabolic substances of a dilator nature.

The pilomotor reactions are lost in approximately the same area as that in which the sweating disappears. Occasionally, small patches of pilomotor effects are observed in the nonsweating areas.

I cannot answer the question about angioneurotic edema because I do not know enough about it, nor can I answer the question regarding herpes zoster.

REMARKS CONCERNING TUMORS IN THE REGION OF THE THIRD VENTRICLE. DR. PERCIVAL BAILEY.

Dr. Bailey presented a series of lantern-slides illustrating the peculiar features of tumors in the region of the third ventricle. In addition to the discussion of

the symptoms detailed in the article appearing in the *Journal of Nervous and Mental Disease* (**69**:1, 1929), the following points were emphasized:

1. Peripheral manifestations of von Recklinghausen's disease are often associated with a peculiar type of glioma (spongioblastoma unipolare et bipolare) involving the optic chiasm and the adjacent wall of the third ventricle.

2. Among the visceral manifestations provoked by tumors in this region should be reckoned angioneurotic edema.

3. Ventriculography is useful in differentiating between tumors of the third and the fourth ventricle if properly done and interpreted. For this purpose, the method of Balado was recommended, in which the roentgenograms are made with the head hanging backward and below the level of the body. Dr. Bailey also insisted that the passage of air or dye freely between the lateral ventricles does not necessarily mean that the foramens of Monro were patent, since large holes are often present in the septum lucidum.

4. Tumors in the region of the third ventricle (tumors of Rathke's pouch excepted) sometimes are much improved by roentgen radiation.

The complete presentation was published in collaboration with J. F. Fulton.

DISCUSSION

Dr. Max Peet, Ann Arbor, Mich.: In this discussion of tumors of the third ventricle, I wish to mention briefly the case of a girl, aged 14, who had had diabetes insipidus and was thought to have pituitary tumor. The output of urine had been carefully watched, and it had not decreased under pituitary therapy. Three weeks before the patient came to us, the symptoms of diabetes insipidus spontaneously disappeared. The visual fields and sella turcica were normal. She was sleepy and soon paid no attention to what was going on about her. I found no evidence of a pituitary tumor and accordingly did not advise operation. The somnolence became more marked, and finally coma supervened. About twenty-four hours before the patient died, vasomotor phenomena, evidenced by color changes typical of Raynaud's syndrome, appeared, first in one foot. About an hour later, the same Raynaud's syndrome appeared in the other foot, and within a few hours it was symmetrical in both hands. No other change was observed and blood counts showed no change. We did not make a thermal examination. There was no gross evidence of tumor at autopsy, but on dissection of the brain we found a tumor destroying the tuber cinereum. It had caused no hydrocephalus and had not pushed up into the third ventricle. The symptoms suggest a terminal invasion of the sympathetic center with changes in both hands and feet.

For several years, we have been using both anterior and posterior positions in making ventriculograms. Sometimes, when the third ventricle does not fill, it is because of insufficient air rather than of a tumor of the third ventricle.

I wish to know whether Dr. Bailey is doing fractional injections or trying to replace all fluid with air.

I should like to have explained why some of the patients with tumor of the third ventricle die so suddenly. One patient in our series died within an hour after the first symptom, severe headache, appeared. At necropsy, we found a small echinococcus cyst attached to the third ventricle, which did not seem as if it could block the foramen of Monro or the aqueduct of Sylvius.

Dr. John B. Doyle, Rochester, Minn.: In the diagnosis of tumors involving structures in the region of any of the ventricles, fluctuation of symptoms and signs is often of great importance. Not infrequently diabetes insipidus is encountered with lesions in the vicinity of the hypothalamus. That this symptom may be transitory is well known. In a patient who had a tumor of the tuber cinereum there was an intractable diabetes insipidus for a period of two years, which ceased six months before death. I should like to ask Dr. Bailey whether he has an explanation for this phenomenon.

DR. PERCIVAL BAILEY: I never do a ventriculography without trying to get all the fluid out, for I think one always encounters difficulty if one does not. Absence of filling of the third ventricle is the only evidence of tumor in that ventricle. Unless one can see a shadow, one cannot make a diagnosis of tumor. The fact that air passes freely from one ventricle to another is not proof that there is not a tumor of the third ventricle. There are often holes that one can put a finger through in the septum lucidum, and yet the third ventricle may be filled with a tumor mass.

I have no explanation to offer for the cases Dr. Peet mentioned.

In the paper I wrote with Fulton on this subject, we used the title "Symptomatology of Tumors in the Region of the Third Ventricle," which gave us a great deal of latitude. We included only those tumors which lay in the wall of the third ventricle.

I do not know how to account for the sudden death that occurs in these cases, but I have tried to explain it on the basis of a blockage of the cerebrospinal fluid. The fact that one can often alleviate the symptoms by changing the position of the head shows that a tumor may be attached in such a manner as to cause blocking in some portion. I think this is the only explanation possible.

LEPTOMENINGITIS: FORMATION OF MACROPHAGES FROM ARACHNOID CELLS. DR. THEODORE T. STONE.

In cases of early acute leptomeningitis in man, the cells lining the arachnoid and trabeculae may become macrophages. The formation of these cells under the stimulus of the inflammation is essentially a process of enlargement: the nucleus becomes eccentric; the cell detaches itself from the arachnoid and becomes ameboid. These ameboid cells engulf fat globules, inert bodies, cells and microorganisms.

DISCUSSION

DR. ROY GRINKER: I do not think the author is justified in saying that he has found the origin of the macrophages on the arachnoidal membrane. The whole subject has been the matter of tremendous controversy, and such investigators as Maximow, Sabin, Foote and many others who have worked for years on the subject have come to the conclusion that in order to determine the origin of the phagocytic cell the only method that is reliable is that of vital staining. I do not think the slides are convincing; they did not show what part the arachnoid plays in the exudate. The pia and the vascular elements, both in the blood vessel walls and in the hematogenous elements, have not been studied sufficiently to rule out their presence in the sections. The descriptive method can offer no more than what is described in any text on pathology.

DR. LEWIS J. POLLOCK: I wish to ask Dr. Stone whether his conclusions are not considerably derived from a rather mathematical formula. As I listened to the paper, I was impressed with the fact that in those places in which the macrophages were found the arachnoidal cells were not found, and where the arachnoidal cells were found the macrophages were not found.

DR. THEODORE T. STONE: If Dr. Grinker will read my paper after it is published, he will find that the pia and the vessels were studied in detail, and that the cellular elements are fully described. He evidently did not hear me say that there is a definite difference: that the macrophages when stimulated may take on a structural change. Note that a club-shaped nucleus is typical of the arachnoidal change, but that is all we have to go by at present.

Replying to Dr. Pollock, I will say that definite areas of cellular exudates in the subarachnoid space were counted and measured. In the material studied in cases in which the meningeal cellular exudate was studied and macrophages found, the arachnoid was abnormal in that the low flat cell was not present. I would like to know what produced the macrophage and what happened to the low flat cell of the arachnoid.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

GEORGE S. STEVENSON, M.D., *Secretary*

Annual Meeting, New York, Feb. 22 and 23, 1929

LAWSON G. LOWREY, M.D., *President, in the Chair*

That parents frequently bring problem children to a child guidance clinic not so much to help the child as to solve their own problems was one of the revealing notes of several papers. Dr. Frederick H. Allen, of Philadelphia, stressed the wisdom of giving attention to the emotional problems of the parents and their relationship to the child rather than making a direct attack on the child's behavior, troublesome as it may be. This is essential to further progress in the management of problem children and the prevention of juvenile delinquency.

The tendency to look for the causes of juvenile conduct disorders in the parent rather than in the child was apparent from many addresses and the discussion which followed them. Dr. S. M. Hartwell, of Boston, for example, in discussing psychotherapeutic endeavor with young people, laid down the principle that in the child's environment the people whom he knows and responds to are more important as influencers of his behavior than material things and events. In a study of birth and nursing conditions and the personal history of the first two or three years of the child's life, Dr. Gerald H. J. Pearson, of Philadelphia, also found that parental attitudes have far more to do with the formation of a child's personality than actual happenings.

In a paper on the play of social factors in personality integration, Dr. James S. Plant, of Newark, N. J., gave the results of six years' study of 2,500 juvenile delinquents which led him to conclude that the family of today is no longer, can be no longer, the arena for the play of all the various needs of its members, and that the family as a social institution has "withdrawn" from other social institutions. The decline of family life militates against adequate personality development and the proper satisfaction of the emotional life that underlies it. In the face of this situation, the psychiatrist must turn to a study of social institutions and community life, and become less preoccupied with his studies of the individual, since he cannot integrate the personality of the individual without integrating the environment in which the individual lives, moves and has his being.

In the discussion of a paper by Dr. Sanger Brown, II, of Albany, N. Y., on why people fail and become dependent, pointed comment was directed at the tendency, symbolized in the democratic notion that every mother's new-born son is a potential President of the United States, to exalt education without regard to the capacity of the child to profit from it.

An interesting study of crime in the "loop" and adjacent districts in Chicago, showing the importance of environment over that of nationality in juvenile delinquency, was described by Dr. Clifford R. Shaw. Other speakers included Dr. Curt Rosenow, Dr. David M. Levy and Charlotte H. Towle of New York; Dr. Herman Adler, Dr. Andrew W. Brown and Dr. Luton D. Ackerson of Chicago; Dr. H. E. Chamberlain of Minneapolis; Dr. William Healy and Dr. Augusta H. Bronner of Boston; Dr. Karl A. Menninger of Topeka, Kan.; Dr. Howard W. Potter and Dr. Florence Powdermaker of Letchworth Village, N. Y.; Dr. Ira S. Wile and Dr. John Levy of New York, and Dr. Lawson G. Lowrey of New York.

All officers of the association were re-elected. They are: president, Lawson G. Lowrey; vice-president, Augusta H. Bronner; secretary-treasurer, George S. Stevenson; councilor, Karl A. Meninger, and editor, Herman M. Adler.

The next annual meeting of the association will be held in New York, on Feb. 21 and 22, 1930.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 22, 1929

C. A. PATTEN, M.D., *President, in the Chair*

CERTAIN FAILURES IN THE ACQUISITION OF WRITTEN LANGUAGE: THEIR BEARING ON THE PROBLEM OF CEREBRAL DOMINANCE. DR. SAMUEL T. ORTON.

The restriction of the material herewith presented to that derived from written language has been felt essential because of the limitation of time. Studies of over 200 cases of reading disability (strephosymbolia) seem to have placed the condition on a firm basis as a clinical entity. These cases constitute a group in which the reading facility is one year or more behind the placement of the child in school and below that which would be expected for his accomplishment in other mental tests. At least 2 per cent of the children in the schools studied have shown a degree of retardation in reading markedly out of proportion to their accomplishment in arithmetic and their ability in all other lines. In some school situations the number has risen to fully 6 per cent or more. It will not be possible for me to go into the details of the factors determining this higher percentage, but in general I think that this probably refers to the method of teaching used in the individual school. In one school situation where the children were taught by the method of sight reading reenforced by the phonetic training of those who did not learn readily by sight, approximately 2 per cent of retarded cases were found. In a comparable group of children in another community where methods of sight reading were used solely and where the child was not permitted to learn the letters of the alphabet until he had learned to read 90 words by sight, 6 per cent or more were found to be so retarded.

The problem of selective retardation in reading is characteristically shown by marking off the child's accomplishments in the form of an educational profile that shows a curve incorporating his chronologic age, his school placement, his mental age, his accomplishment in arithmetic and in spelling and reading. By this graphic method it is possible to show that many children exhibit a highly selective blockage in the acquisition of reading and spelling. This is not a problem of intelligence per se since it can be shown, even by the probably inadequate test which the Binet method offers in these cases of special disability, that the whole range of intelligence is represented in children who do not learn to read readily. Indeed, it is not infrequent to find, at least in the lower grades of school, a child who shows a superior mental ability by the Binet standards, ranging to an intelligence quotient of 125 or more, who yet has met an almost insuperable obstacle in learning to read. These children frequently show a good emotional adjustment to their social environment, many of them having done exceedingly good work in nursery schools, kindergarten and preschool groups, only to meet with a selective obstacle on entering the first grade where reading is for the first time a part of their duty.

Since the aim of education in the schools is that of planting the proper or correct responses in the child's mind, the major aim of teachers at large is that of correcting any errors that a child may make. For that reason the major part of the symptoms of the reading disability are disregarded. The errors, however, may be looked on as the symptoms of the obstacle to the acquisition of reading and an analysis of such errors forms the proper approach not only to the understanding of the obstacle but also to the problem of retraining. I pointed out this fact in my paper, "Word Blindness in School Children," in 1925. This analysis of error was carried much further, during 1926 and 1927, in Iowa under a grant from the Rockefeller Foundation that made possible an extensive study of a large series of these special cases.

Practically all cases of the reading disability in which there is a highly differential retardation in the capacity to read, yet in which there is evidence of adequate

mentality for that task as evidenced by other tests, are characterized at the earlier stages by a confusion between such reversible symbols as *b* and *d*, and *p* and *q*, while there is loose association between the visual symbol as presented and its corresponding sound, by a strong tendency toward sinistrad progress within the word or sinistrad reading of the word as a whole, by a certain fairly definite facility in reading from the mirror and in some cases by a considerable facility in mirror writing also. The confusions that exist between *b* and *d*, and *p* and *q* are apparent. It is obvious that the reversed or mirrored form of a *b* in lower case type constitutes a *d*, but there is no method of identifying a confusion that would arise between the correctly oriented lower case *a* and its mirrored counterpart. There is, however, a striking inconstancy in the building of associations between the individual visual symbol and its proper sound. This is most obvious in letters with more than one sound, as in the vowels and in *c* and *g*. These confusions and lack of associations are consistently found, of course, in practically all small children at the beginning of their educational progress in reading, but they are carried over to a much greater degree in children who show a true specific retardation in this subject. Children who are far along in their accomplishments at school, indeed, children up to high school grade, may have serious defects in the association between symbol and sound. The sinistrad progress may be that of the whole of a short word, as when "was" is read as "saw," "on" as "no," "not" as "ton," and so forth; it may be merely the inversion of a pair of letters, as when "calm" is read as "clam" or "from" is confused with "form"; or one syllable may be read in the dextrad direction and the other in the sinistrad form, as when "reared" is read as "reader," or "tarnish" as "tarshin." Again, both syllables of a two-syllable word may be read in the proper order but both in the sinistrad direction, as when "tarnish" is read as "ratshin"; each of two syllables may be read in the dextrad or proper direction but may be assembled in sinistrad sequence, as when "repast" is read as "astrep"; or merely the initial letter may take its proper place, all the rest of the word being reversed, as when "tomorrow" is read as "tworrom."

The lack of facile association between the symbol of a vowel and its correct sound gives rise to many further errors in reading. When this condition, as well as the confusion between *b* and *d*, and *p* and *q*, is combined with a tendency to omit parts of words or to reverse other parts, one finds many bizarre errors of reading. "Began" may be read as "bang," "named" as "made," "card" as "bark," "squirt" as "sipert," "target" as "ratchet," and "tarnish" as "trench." Some interpretation is required to see how these errors come in. The first inclination toward a misreading of this kind would be to find no logic or rule underlying it. However, when one sees a child attempt to read the word "target" first as "tegr," omitting the "at," and then, in an attempt to harmonize that with some word orally known, call it "tiger," one begins to understand the genesis of such mistakes.

These tendencies toward reversal and reading in confused order have been looked on by some writers as derived from a tendency toward improper movements of the eye. They have also been associated in certain discussions with a selective use of the left eye for fixing at a distance (left-eyedness). This vision of the matter seems, however, not only to be superficial but to be largely negated by the fact that many similar errors are shown in the children's recall of these words as exhibited in written spelling. Errors of oral spelling are excluded from the present discussion because of restrictions of time. Errors in written spelling, however, show mistakes comparable to those outlined for reading. *B-d* confusions in written spelling are exceedingly common. Not only may the *b* take the place of the *d* at times, but apparently they are often interchangeable. A boy writing "rudder" may use one correctly oriented symbol and one reversed, thus producing "rudber," or in writing the word "baby" produce one *b* and one *d*. Reversals of the type quoted among disturbances in reading are also frequent; for example, "bewten" for "between," "dirfence" for "difference," "dierct" for "direct," "libtery" for "liberty," "palying" for "playing," "statoin" for "station" and "Enlgand" for "England."

Other errors of a variety of types show themselves in writing, many of them derived from the phonetic memories of the words, but many also showing various other sources. One interesting type of error is that of perseveration. This occurs occasionally in a series of words, when the child has encountered a word in which he has made a mistake or feels some insecurity in the spelling that he has offered. For example, the child who spelled "fight" "f-i-c-h-t" apparently was still thinking of that word when she spelled "buy," the next of a series, "b-u-g-h-t." Again, after correctly spelling "eight," a child was given "afraid" and spelled it "a-f-r-a-i-g-h-t."

A still more complex associative process leading to a misspelling came out recently in a test of a small girl who spelled "uncle" "w-a-l-c-e-l." The origin of the first syllable of this composition was obscure until the mother explained that the child had an Uncle Walter who was familiarly known as Uncle Wal. Even in this recall, however, the reversed sequence exhibits itself in that "wal" appears ahead of the fraction of "uncle."

Disturbances of this nature may exist in spelling as more or less of an isolated disability. When there is a striking reading disability, misspelling is almost always present, but as time goes on, many of these children accomplish a certain degree of reading through special effort on the part of themselves or their teachers or at home, and apparently establish the association from the visual intake to the word sounds and hence to the meaning. However, the association in the reverse order from sounds of words as called up by volitional memory or as presented orally by the teacher do not form a quick and secure association with the visual symbols that should represent them, and striking failures in spelling may therefore persist.

A still further functional separation in this sphere seems to be possible in the differential defects that sometimes are to be observed between written spelling and oral spelling. A child who had been the leader of her class in spelling in the Texas schools and who had moved to Iowa was failing consistently in spelling. On inquiry into the situation it was found that all of her spelling in Texas had been by oral recitation, whereas all of her spelling lessons in Iowa were written. Obviously, the associations that were formed between the sequence of letters in a word were adequate as a control of speech but were not carried over so readily as a control in writing.

Mirror reading, which has been mentioned as one of the symptoms of strephosymbolia, correlates fairly closely with retardation in general reading. In a large group of first grade children the normal readers required four times as long to read simple material in the mirror as they did viewing it directly. The children who were slightly retarded in reading, but not seriously so, required about three times as long. Those of the second grade of severity of the handicap required about twice as long, while for those with the most severe obstacle the reading time in the mirror was about equal to the time required for reading a comparable passage by direct examination. Indeed, in one or two cases the children were able to read with greater fluency and ease with the mirror than without. Not only does this capacity for mirror reading seem to correlate directly with retardation in reading progress, but it disappears progressively as the child learns to read. When in the first grade, the children with an extreme degree of the handicap read with approximately equal speed with the mirror and without. By the time they have accomplished second grade capacity in reading the ratio is 1 : 1, and by the time they are reading with the facility of an average fourth grade child, it has climbed to 1 : 3.2. Meantime the ratio of times between mirror reading and reading without the mirror in the normal children who have reached the fourth grade has increased to over 1 : 8. The tendency toward easy acquisition of either the mirrored or the direct form is probably universal in all children in the lower grades. In those who are suffering from the reading disability, however, the relative ease of reading in the mirror is demonstrably in direct proportion to the degree of their disability.

Mirror writing is not so directly associated with the reading disability. It is often present, however, in first attempts at writing, and it frequently persists as

an occasional reversal of a letter within a word. It rarely exists as the only facile method of writing. A medical student, aged 21, whose writing was so exceedingly poor that he himself could not read it, was tested for all four possibilities in writing, that is, to the right with either the right or the left hand, or to the left in mirrored form with either the right or the left hand. He was able to write with fair facility and with no previous practice only when using the right hand in mirrored form.

In cases of reading disability it is possible to demonstrate that the degree of difficulty in acquiring reading is not directly related to the general intellectual capacity. While many slow readers have defective minds, others fall in all ranges of the intellectual scale. They are not to be interpreted, therefore, as defectives. Furthermore, many of them are exceedingly apt with their hands. They are at least the equal of an unselected group of good readers, and a few show marked ability in visual manual control in spite of complete inability to understand the printed word. Again, many of these children handle pictorial material exceedingly well. Here again one finds a range of distribution, without relation to the degree of the disability; indeed, in my most severe case of strephosymbolia the patient was able to make an excellent record for himself in all material dealing with pictorial images. In the Healey pictorial completion test no. 2, for example, he made a record equaling that of the highest 10 per cent of normal adults. From these facts one must conclude that vision is normal as a motor guide and that higher elaboration of visual material is adequately carried out up to the pictorial level; in other words, this disability rests on a selective interference with association at the third or language level of cerebral elaboration. There is a faulty linkage between the printed symbol and its sounds, which results in an inability to read, and between the sounds and the symbol in reverse order, resulting in an inability to spell. It is of particular interest that it is also at this third level of cerebral elaboration that there enters the problem of unilateral cerebral dominance. The data derived from histologic and myelinogenetic studies indicate three fairly distinct structural levels. At the first of these cortical blindness has been related, at the second mind-blindness, and at the third word-blindness. In support of this view I would like to add the evidence of good manual control and good use of pictorial material with complete disjunction at the language level, as shown by these cases of strephosymbolia.

In interpreting these observations it is necessary to bear strictly in mind that there are rather striking differences between the functional and anatomic relations of various parts of the brain mechanisms. All parts of the brain are structurally strictly antitropic, but some of the functions apparently are unilaterally independent in their activity, while some operate by fusion and others apparently by unilateral dominance. In the motor zone it is obvious that the two hemispheres have a unilateral and independent, although antitropic, relationship. Thus, while the right and left motor zones are mirrored counterparts of each other, each operates in control of one hand only. This obviously is a physiologic necessity and is borne out by observation of the unilateral paralysis that follows a unilateral lesion in this zone. A similar unilateral and independent relationship exists in the epicritic cortices of the postcentral zone, and again one sees that this is a physiologic need. It is important to the organism not only that it recognize a threatening sensation of temperature applied to the thumb, but also that it recognize which thumb is threatened. To secure proper responses on the part of the two arms, the record of their experiences must be written separately in the two hemispheres. This need, however, is not apparent in vision or audition. To enable the animal to make the proper response to a single source of light or to a single source of sound it is important that this be not represented in the brain as an image received in either eye or either ear, but that it be interpreted by the brain as of its single actual source. Such a result might be accomplished by either of two methods: (1) that of rivalry in which the sensory experience of only one hemisphere at a time was operative, and the other was elided, or (2) that of fusion in which the contemporaneous incidence of a stimulus in each hemisphere was interpreted in consciousness as a single experience. It is probable that rivalry operates in animals without

an optic chiasm, and that in such an animal one hemisphere maintains the focus of attention temporarily and hence controls responses at that time, and that when a stimulus of sufficient intensity reaches the other hemisphere it gains the responsive control by rivalry with the first. Sherrington's extensive study of binocular vision by the "flicker method" seems to have established adequately that in human vision this is not the case but that the two hemispheres work together, this process of fusion resulting in the arousal of a single conscious impression from bilateral stimulation. Moreover, bilateral lesions are held to be essential for the destruction of either visual or auditory functions at both the first and the second levels of elaboration. One must therefore look on these two levels of auditory and visual functions as bilaterally equivalent. At the third or associative level, one finds some dispute. This is the field in which both Head and Marie recently challenged the accepted version of a pure unilateral dominance. I think it must be held, however, that the majority of studies of aphasia that have been made are to be looked on with doubt. Under current methods of training, many children who have a tendency toward left-handedness are unquestionably shifted to the use of the right hand in practically all manual operations, including writing, and hospital records usually take cognizance only of the hand used in writing to determine handedness. It seems obvious that the question of the initial or physiologic preference of any given person for the use of one hand or the other cannot be adequately established thus, and that the determination of the dominant hemisphere in many cases recorded in the past, therefore, rests on an insecure basis.

While one must acknowledge that the effects of training may effectively mask the native physiologic bent of the person, and hence must recognize that much of the confusion in the literature of aphasia may result from this fact, yet one can say that a unilateral lesion is sufficient to interfere with language. One must assume, therefore, that there is a striking difference in the functional capacity of the two hemispheres. There is, however, no comparable structural difference. The two hemispheres of the brain are approximately equal in size, and while minor structural differences may be hidden, there are none of such rank as those seen in the functional expressions of aphasia. The theorem of neurobiotaxis has led to the conclusion that nerve cells do not reach their full development except when they are exposed to stimulation. The fact that the third level areas of the nondominant hemisphere of the brain have developed practically equally with those of the dominant leads one to assume that sensory irradiation must have taken place in this side as well as in the dominant hemisphere. If they have been equally irradiated, one must further assume that records have also been left in the nondominant hemisphere, and that the normal habit of leading exclusively from one hemisphere for the expressions of this level, that is, speech, writing and meaningful gestures (sign language) is of physiologic nature. If, on the other hand, there should be a failure to establish a clearcut habit of leading from one set only of these duplicated records and a persistence of the records in the nondominant hemisphere, one would expect to find exactly the symptoms that have been demonstrated as constituting the clinical entity of strephosymbolia, that is, confusion between reversible symbols, a tendency toward sinistrad sequence and a facility in mirror reading.

This forms, as will be seen, a physiologic rather than a pathologic hypothesis of the obstacle to the acquisition of reading in these children. One may therefore assume that this disability would respond to proper methods of training. The fact that these children have not learned to read when exposed to the ordinary methods of training at school merely indicates that the methods in ordinary use do not suit their particular method of acquisition — not that these children cannot be trained by methods that are adapted to their cerebral patterns. This has led to an attempt to establish adequate associations between the visual and the auditory, and for this purpose it has seemed that kinesthetic reenforcement offers the greatest promise for two reasons: 1. It is next to impossible when using the kinesthetic method to reverse the direction of travel through the word. 2. The kinesthetic implants in the brain are strictly unilateral, and hence one may tentatively

assume that one is encouraging the selective unilateral use of one hemisphere when kinesthesis is used. For this purpose I have recommended the tracing of a pattern at which the child looks while saying the corresponding sound or sounds.

I will not be able to give details of retraining experiments here, but it may be said that in many individual children striking changes have taken place not only in the capacity to read but also in the types of error that they make in their efforts at reading. A girl in the third grade of a high grade private school, had acquired less than the average reading capacity that one would expect in a first grade child. She knew relatively few of the sounds of the vowels, had confused some of the consonants and could read practically only the simplest two and three letter words. In other respects her intelligence seemed to be average or even superior. Her work in arithmetic was good, her social adjustments, except for her reactions against the reading disability, were adequate and she seemed to be unusually quick in learning most things by ear. In eleven months of consistent retraining, largely by means of the kinesthetic reenforcement, this child not only had regained all of the lost time of her first three years but had reached her actual placement in class which by that time was the fourth grade. In other words, in one year of special training she had acquired four years' skill in reading after having failed of any acquisition during three years of training by usual methods. Other children have shown comparable advance.

One factor of the disability that I think must be clearly recognized is the effect on the personality of the child. This forms a potent part of the obstacle and one that must be taken into cognizance in treatment. Several reaction patterns of the children to the situation in which they find themselves when others of their class are reading with much greater ability than they, have been observed. In some instances one finds striking emotional blocking; in others marked feelings of inferiority; in a few a paranoid reaction, and in many an increasing apathy toward educational work. Those reactions must be considered, if retraining work is to be made effective. The child himself must be led to understand that the disability is not engendered solely by his stupidity, by his inattention, or by his unwillingness to apply himself, but is a special obstacle of organic nature that can be overcome only by application on his part. Usually the reaction of relief that comes to the child with this view is tremendous and the willingness of application in an effort to overcome the disability is a great asset to the program of retraining.

DISCUSSION

DR. CHARLES K. MILLS: Dr. Orton is to be congratulated on the splendid work that he has done not only for Iowa but for every state and community in every part of the world that is striving to arrive at measures of practical value in elementary education. If I correctly understand the matter, my discussion of Dr. Orton's paper is to be from the standpoint of cerebral localization. My remarks, in other words, must be concerned with different so-called centers of the brain and their association and, in addition, with the anatomic and physiologic results of the use of these centers and tracts.

The acquisition of brain power follows Darwin's laws of pangenesis, and the subject of reversion is extremely important in this connection. This reversion can take place after many years or after many generations.

I have had numerous instances of a tendency to return to ancestral language. One of the most important of these was the reciprocal understanding of a Bretonne woman and a servant from the southwestern part of Ireland, which brings to mind the fact that in bygone geologic ages France and Ireland were terrestrially connected.

With regard to language reversal, of which Dr. Orton has had so much to say, I have observed numerous examples. These may be of the entire word, of syllables or even of letters, but they are especially shown in what might be termed syllabization. The mistakes are the result not of serious impairment or destruction of the brain, but of a tendency to confusion in associating the mental images of words or of their constituent parts.

I believe with Dr. Orton that educators have departed too much from what is sometimes spoken of as the old fashioned methods of teaching. Spelling books and etymologies have been in large part banished from the schools and, instead, imperfect methods, of which the so-called "see and say" method is an example, have been substituted. Phonetic methods may be necessary to a certain extent, but the derivation and definition of the meaning of words should be taught if the use of words and phrases is to be understood.

In the explanation of the disorders or difficulties of language exhibited in the children whom he studied, Dr. Orton lays great stress on the effects of interference between the activities of the two cerebral hemispheres. The left hemisphere in the ordinary right-handed person is the leading hemisphere for speech, writing and reading. In the left-handed, the right hemisphere has a tendency to take the leading part. Because of the manner in which the ordinary school education is conducted, the two hemispheres struggle with each other for dominance and give confusing results.

Many facts seem to indicate that the right cerebral hemisphere takes a larger part than the left in emotional life. Even the most extreme localizationist recognizes that the brain acts as a whole as well as in its separate parts.

Some of the persons to whom the term moron is loosely applied may be permanently defective, but they are not all of this class. In the cases of some morons, as in a number of children examined and reported by Dr. Orton, the mentality is delayed rather than destroyed. Many of the so-called morons may at the bottom be possessors of sound brains.

The whole of the dual and complicated cerebral apparatus may be more or less involved in Dr. Orton's strephosymbolia or twisted language group.

Closely related in the cerebrum to the isolated centers for words, letters and numbers, all of which are separately represented, there is an area for object imagery, sometimes spoken of as the area of architectonic form. Some of the cases studied by Dr. Orton illustrated the presence of this object area in the cerebrum.

Studies like those made by Dr. Orton, while of world wide or international interest, are particularly of value to this conglomerate land.

The question of left-handedness or right-handedness and of mirror writing necessarily comes into the discussion of Dr. Orton's paper on failures in written language, whether these failures are in spelling, construction, pronunciation or of whatever sort.

DR. W. G. SPILLER: Dr. Orton stated a fact generally recognized, namely, that the speech centers are in the left cerebral hemisphere in right-handed people. He examined a large number of microscopic slides, prepared by taking sections from corresponding parts of each hemisphere and, as might be expected, he found no difference in structure in the sections from corresponding parts of the two cerebral hemispheres. He concluded that in normal persons the speech functions of the right cerebral hemisphere are elided. In abnormal persons this suppression does not occur, and the speech zone of the right cerebral hemisphere is responsible for mirror writing, reversion of syllables, etc.

He also stated that the motor cerebral cortex supplies only the opposite side of the body. The existence of an ipsolateral pyramidal tract, as well as of a crossed pyramidal tract, cannot be doubted. In 1895, I carried out an investigation, by the Marchi method, of the degeneration in the spinal cord in hemiplegia resulting from a unilateral cerebral lesion, and clearly demonstrated the existence of an ipsolateral pyramidal tract in the lateral column of the spinal cord, which probably varies in size in different persons. The function of this ipsolateral pyramidal tract is usually elided.

I know of two cases in which a person was unable to perform isolated movements of one side of the body. I saw the first case in the National Hospital in London, in 1913, at the time of the international congress. The second case was reported by Dr. Burr. Whatever movement either of these persons made with one upper limb he was obliged to make also with the corresponding lower

limb. It seemed to me that the best explanation for this phenomenon was that the function of the ipsolateral pyramidal tract in these cases was equal to that of the crossed pyramidal tract, and that any impulse originating in the motor cortex of one cerebral hemisphere was distributed to the pyramidal tracts of both sides of the spinal cord.

DR. SMITH: I should like to have Dr. Orton mention some of the psychiatric aspects of these cases. I saw several patients in this work. Many showed definite changes, some having even confusion and emotional blocking.

MR. JOHN G. KIRK (Director of Commercial Education, Philadelphia Public Schools): The Division of Commercial Education has general supervision of the commercial and handwriting work in all school grades. One of the problems confronting the public schools is whether or not the left-handed child should be taught to write with his right or his left hand. This is a right-handed world and the left-handed writer in school, in business and in life is a decided disadvantage so far as lighting, desk arrangement, instruction, etc., are concerned.

We made a study of a number of records and found that members of the medical profession did not agree on any one plan of procedure for handwriting. A study was made over a period of four years in Elizabeth, N. J. All incoming pupils were taught to write with the right hand, and all left-handed writers in the school were changed to right-handed writers. During the four year period only two cases of stuttering were discovered. A special study of these cases revealed that the pupils had stuttered before the change. This and other studies reveal that change of writing hand is only one of many possible theoretical factors in the cause of stuttering.

We should like to have the reaction of Dr. Orton to whether or not we are justified in having a left-handed child adapt his right hand to writing, or whether he should use his left hand and risk injury to his eyes on account of the lighting arrangement of the school desks. In junior and senior high schools and college the student suffers further inconvenience by being forced to assume an incorrect posture when taking notes on a "table-arm chair." We have found that children who change hands write remarkably well and exhibit no signs of stuttering or other defects of speech. We are always willing to follow the suggestions of the research results of medical study, as we want to do what is best for the child.

DR. MCCONNELL: My mother, who was a school teacher, was left-handed, but she wrote right-handed. I am right-handed, but in college I met with an accident to my right arm and learned to use the left. Later, I played ball with the left hand rather than with the right. Dr. Agnew made us learn to perform surgical procedures with the left hand as well as the right. My son is naturally left-handed, but writes with his right hand. His writing is atrocious. He does everything else with his left hand. My daughter is left-handed. When she went to school, the attempt was made to teach her to write with the right hand. She produced mirror writing and was therefore allowed to continue with the left hand. She now writes with both left and right hands.

DR. SAMUEL T. ORTON: Dr. Mills has brought to the fore the problem of confusing children with special disabilities with those who have a true mental defect. With teachers who find that a child has great difficulty in learning a particular subject there seems to be a tendency to consider this as evidence of a general mental defect. These special disabilities, such as a measurable defect in reading, often accompany a general mental enfeeblement. Psychometric examinations applied to children with striking confusions in reading will show that this disability is by no means limited to the bright children but occurs also in those of inferior mental grade. It can be definitely demonstrated, however, that many children with average or even superior minds suffer from this isolated disability of the learning process. I have seen children suffering from a considerable degree of this disability who seemed at first stupid in all their reactions to school work until efforts at retraining were begun. As their difficulty was gradually overcome, however, they evidenced not only good effort but good intellect. It is important in this regard, I think, to recognize that while one may encounter an isolated disability in one func-

tion, as for example, in reading, one may encounter combinations of one or more of the various factors in any one child. A child was brought to me who showed striking confusions of direction such as characterize the reading disability, who also was rather slow in the development of speech and who had had a considerable degree of developmental apraxia during his earlier years. This child had been in school for three years; he knew none of the letters of the alphabet, could not read at all and had shown a decisive tendency toward mirror writing, together with these other defects. I had to say to his mother that I did not know whether the child could be retrained or not. Had he exhibited only one of these disabilities, I am sure that it could have been corrected by training. In the presence of them all, I was constrained to tell the mother that I did not know how much could be done for him. This child had been turned away from school after a psychometric examination rated him as a low-grade moron. The mother, however, after only six weeks was able to teach the child the alphabet and to write the symbol from the sound or the name of the letter, and had begun with short words. Progress was slow and difficult, of course, but definite.

Dr. Spiller has brought up the question of apraxia in connection with the establishment of dominance. One little girl was brought to me with the complaint that she was exceedingly clumsy and could not learn dance steps or meaningful gestures to accompany speech. She was a left-handed child and seemed to have a great deal of confusion as to which foot to start with in the dancing measures. On observing her, I found that when she looked directly at the teacher, she exhibited considerable uncertainty and doubt, but that apparently she could follow movements that were made before the mirror. I suggested to the teacher, therefore, that she try to train the child in front of a long mirror. Progress by this method was striking.

Dr. Smith spoke of the emotional factors in these children. Dr. Sprague and myself, after the study of rather a large series of cases, have come to the conclusion that the emotional factors are of great importance and that in the majority of instances they are definite reactions to the presence of the disability. These children have met an obstacle. They do not understand why they cannot learn to read as readily as they learn arithmetic. The obstacle is not obvious, as a speech defect or a true defect in vision or hearing would be. Consequently neither the teachers nor the parents understand why they are not making better progress. Some type of emotional reaction and adjustment is therefore to be anticipated. We have found that there are four striking types of reaction to the disability. By far the greater number of children develop a strong feeling of inferiority. With this often come many masking reactions, such as casualness, a defensive apathy or an overassertive boastfulness. The second largest group are those who develop a striking apathy toward school work, which usually extends over into other school topics than reading. Two smaller groups of emotional reaction patterns were noted. One of these was the paranoid group who tend to blame all of their failures on the school teachers. This apparently comes to the fore more strikingly in children whose parents have the same feeling, that the fault lies not with the child but with the teachers. The second group comprises those who show a striking emotional blocking. In such a child any attempt at query about the school work is met by either an immediate mutism or a prompt reply of "I don't know." Not infrequently a child with this reaction becomes strongly blocked in all types of emotional expression.

Mr. Kirk's questions are somewhat more difficult to answer because in every instance the problem presented by such a special disability is one for individual analysis and solution. Mr. Kirk apparently feels that by virtue of the numbers studied, it is safe to recommend the enforced training of every child for right-handed writing. On the other hand, I have seen stuttering result frequently from such an enforced shift. Not infrequently the stuttering clears up rapidly if the child is permitted to go back to the normal hand for writing. I recently saw a child, aged 3½, whose parents brought him to me with the statement that he had been stuttering for about two weeks. Two weeks before the stuttering began,

he had had a hard fall and the parents were apprehensive for fear he might have suffered an injury to the brain. I asked concerning the child's handedness and the mother responded that he was clearly right-handed. The father had some lingering doubts and thought that the boy was about half and half. I suggested a week's close observation. At the end of that period the child was brought back with a report from the parents saying that he did only three things with his right hand: eating, using a spoon and digging in the sand, in all three of which he had been taught by an adult. In all things that he did spontaneously, in other words, those in which the training factor had not entered, his selection was consistently that of the left hand. I advised a complete retraining for the use of the left hand in everything. Within two weeks the stuttering had practically cleared up. While I appreciate that many left-handed persons can be taught to write with the right hand without this result, I feel that there is a chance of incurring a true disability, such as stuttering, when an enforced shift is made. And I think further that it is doubtful whether the right hand ever becomes as facile as would the left hand in those children who are physiologically intended to be left-handed.

A Case of Focal Cortical Lesion Associated with a Speech Defect. Dr. C. W. Irish.

This is a case of motor aphasia with partial recovery but with residual stuttering, due to an area of softening at the lower part of the left motor area just posterior to Broca's area.

History.—A white man, aged 70, was admitted to the neurological service of Dr. D. J. McCarthy, Philadelphia General Hospital, on Feb. 8, 1924, with a history of sudden paralysis of the right side of the face and of a motor aphasia fifteen years previously. A residual speech defect persisted during the rest of his life. He entered the hospital on account of a gangrenous condition of the right toes. His past history had no relation to this condition. He had anthrax seventeen years before and a skull fracture nine years previously. His eyesight had been failing for several years, with the formation of cataracts in each eye. He had frequent frontal and occipital headaches relieved by medicine.

Examination.—The patient was poorly developed and undernourished. He had bilateral cataracts causing partial blindness. There was ptosis of the right eyelid and drooping of the right corner of the mouth. The tongue protruded in the midline; the soft palate was fixed on the right side. There was a definite dysarthria. The deep reflexes were prompt and equal. Sensation was normal. There was some weakness and incoordination in the lower extremities. The chest was emphysematous, the heart was hypertrophied and the blood vessels were sclerotic. The toes of the right foot were discolored and cold. No pulsation could be detected in the dorsalis pedis artery.

Course.—Following some improvement in the condition of the foot, the patient suddenly became stuporous a few days after admission; the left foot became gangrenous and the patient died fifteen days after admission to the hospital.

Laboratory and Necropsy Reports.—Examinations of the spinal fluid and blood gave negative results except that the blood sugar content was 190 and 125 mg. on two occasions. The urine was normal.

The brain showed a sharply defined area of softening in the lower part of the left motor area, extending from the central fissure to the triangular portion of the opercular area, measuring 3.5 cm. in width, with its base sharply defined by the sylvian fissure and extending 4.5 cm. toward the vertex. The walls of the cavity were smooth and extended 2.5 cm. to lie against the external capsule and claustrum as shown on horizontal section. This area of softening was probably due to a thrombosis of the ascending branch of the middle cerebral artery.

This case, with several others, was reported by Drs. George Wilson and N. W. Winkelman in the *Atlantic Medical Journal*, February, 1925, under the subject of "Segmental Cerebral Monoplegia of Vascular Origin."

DISCUSSION

DR. N. W. WINKELMAN: Cases of this kind are rather rare. I do not think that we have more than two dozen in all.

DR. TEMPLE FAY: I recently saw two children in whom a speech difficulty began after they had learned to speak correctly; the vocabulary diminished to the point where there was a decided impairment and at times great difficulty of speech. An encephalogram showed definite cortical atrophy in the left temporoparietal region by the large collection of air. In a boy, aged about 7, there were two distinct depressed areas in the angular gyrus region as well as a rather large air space around the island of Reil.

DR. ALFRED GORDON: At one of the last meetings, last year, I showed a specimen in which there was softening in Broca's region. The lesion was limited strictly to that area. As to the localization of aphasia, literature on the subject shows that in some cases Marie's contention is correct, and that in other cases it is just the opposite. I have anatomic cases in which Marie's view could be accepted in toto. In the last specimen to which I refer, however, the classic conception remains unaltered. The subject is still complex. A still greater number of specimens will be required to decide the problem of localization of motor and sensory aphasia.

DR. A. M. ORNSTEEN: I know the patient in the case to which Dr. Fay referred. The encephalogram showed atrophy over the left temporoparietal region. It was much easier for this boy to spell a word than it was to wait until the word had come to his mind.

A CASE ILLUSTRATING A READING DISABILITY. DR. RUTH BURR.

This case, illustrating a reading disability, resulted from frequent changes of residence during early school years and from certain emotional factors.

History.—The boy, aged 15½ years, who was in the seventh grade, showed poor school work — failure in spelling, grammar and history and marks below the average in all subjects — daydreaming of inventions and mechanical devices, and absent-mindedness. The family history is of interest in a number of respects. The paternal great grandfather, grandfather and father died of angina pectoris. The maternal grandfather died of tabes dorsalis, and the maternal grandmother had symptoms of paresis. Both paternal and maternal grandfathers were mechanical engineers of note, while the father was also an inventor and mechanical engineer, as well as a professor at Drexel College. The immediate family consisted of three children: one seven months' baby that died within a few hours, the mother being very ill at the time, the patient, and another boy two years younger.

The patient had a normal birth. He was breast fed only for three weeks and although he had subsequent nutritional difficulties, these cleared sufficiently in one year to render him normal. He had the usual diseases of childhood and suffered from nocturnal enuresis until the age of 12. No difficulties were noted in connection with the child until he began to attend school. Owing to the father's profession, the family were continuously moving. From 1917 to 1921, the patient was in seven different schools and under as many different school systems. The family moved between Los Angeles, St. Louis, Pittsburgh, New York and Philadelphia. He was kept for two years in the first grade, then progressed to the third, was demoted to the second, progressed again to the third only again to be demoted to the second. Since the death of the father, in 1922, the family have remained in Philadelphia; here he was not subjected to further transferring and progressed regularly except for the repetition of the sixth grade. He is now in the seventh grade in which all his work is below 70.

In addition to the terrific strain of the many changes and his uncertainty in school work, he and all the family were under great emotional tension, owing to the feeling aroused against Germans at the time of the World War. The father was Swiss and the mother German. The German name and the fact that German was spoken in the home put them under suspicion. Although they were all familiar

with English, they found it difficult to speak it. For days at a time there would be no talking in the home. The patient was ridiculed, teased and made to take the part of a Hun in his games with the children. He took this all so seriously that he would beg to be allowed to carry an American flag whenever the family went out on the street.

Physical Examination.—The boy was undersized, poorly nourished and 7.8 per cent underweight, with slightly infected, hypertrophied tonsils. Neurologic examination gave negative results. He was not left-handed. There was no speech defect. Examination of the eyes showed slight hyperopia. The question of whether glasses were needed arose only because of reading defect.

Psychologic Examination.—The intelligence quotient was 94. Because of the patient's superior visual imagery, his excellent reasoning ability and his remarkably high mechanical rating, contrasting with his poor educational achievement which

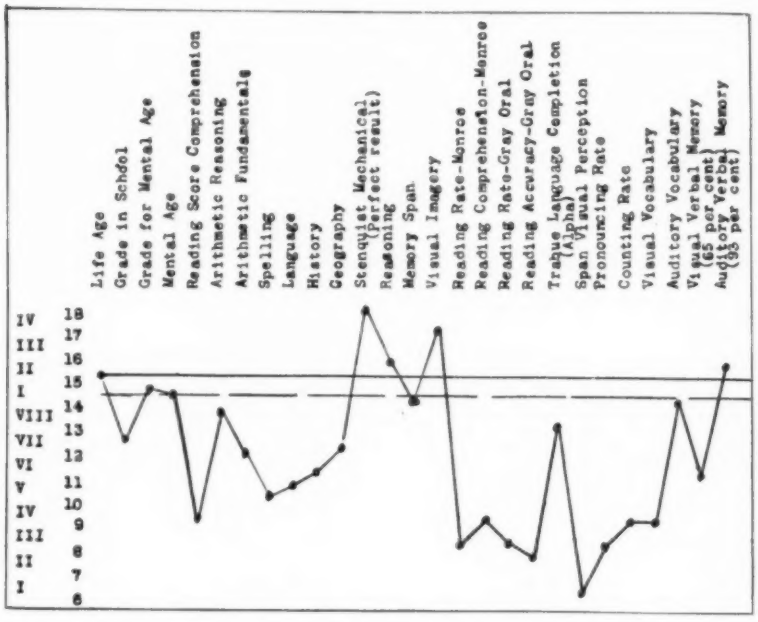


Fig. 1.—Comparative study of life age, mental age and special abilities. The life age (15 years, 5 months) is represented by the straight line, the mental age (14 years, 6 months) by the broken line, and the special abilities by the dotted line. The Roman numerals at the left indicate the grade, the Arabic the age in years.

was inferior for both his age and his mental ability, it was decided to investigate further the cause of these disabilities. The outstanding factor in all tests was his extreme slowness. But even with no time limit the tests showed little improvement.

Psychiatric Examination.—The patient entered into a frank discussion of his personality difficulties. He considered himself intellectually inferior to other boys and recognized his slowness in learning and his failure to grasp quickly new situations. His only satisfaction was unpractical daydreams of motorless ships with wind driven wheel and other mechanical devices. His slowness in learning, difficulty in concentrating, dread of recitations and the fact that he was an older boy among younger ones caused a dislike of school and aided in the development of a feeling of inadequacy. His sensitiveness was extreme. If laughed at he

brooded for the rest of the day. The boy craved leadership, but would not boss and so failed to make an adequate social adjustment. He admired loyalty and efficiency, lacked a sense of humor and was far too conscientious and serious. His seriousness was increased by an emotional hold-over from the death of his father. Throughout the interview the patient overemphasized his shortcomings and minimized his good qualities.

Comment.—The reading disability could be traced along with the development of inferiority as it grew with the increasing intellectual, physical and social maladjustments. The intellectual inferiority had its origin at the time of entrance into school, when he was subjected to seven different school systems. This was the time that he should have received adequate and consistent instruction in reading. Also, his familiarity with German would make it still more difficult for him to learn English. Coincident with these factors was his subjection to a severe emotional strain in being classed as German, condemned and rejected by his playmates. With the school changes and the emotional tension it was impossible for him to become proficient in reading. Owing to his disability he was soon faced with a failure in his school work. The inferiority that was thus beginning found a fertile field in which to develop, for the mother and father had not accepted the child. The mother had always wished to work, and rebelled against establishing herself as a homemaker. The birth of the child acted as an obstacle to her desired ends with the result that she rejected him during his early years.

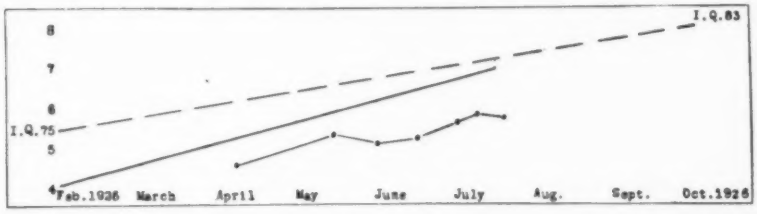


Fig. 2.—The results of remedial teaching. The broken line indicates the Terman group tests, the solid line the Thorndike-McCall reading tests, and the dotted line the McCall reading lessons (average for a group of ten). The numbers at the left represent the grade. Note the two measurements of the intelligence quotient (I. Q.).

His repetition of grades and his demotions made him conscious of his failures. He came to consider himself unable to learn instead of building up a defense reaction. The mother fostered this attitude, for she too believed him mentally defective, although she made intellectual efforts at encouragement, saying that marks did not count. He recognized this subterfuge. His failures were intensified by the mother's great urge to have the boy follow in the footsteps of his father, fulfilling the family ideal that the boy should be a mechanical engineer. He himself would gladly have filled the father's place, assuming the responsibility forced on him by the mother, who was not prepared to support and manage a family at the time of the husband's sudden death. His drive to follow in his father's footsteps made him all the more conscious of his failures to do so.

His physical underdevelopment threw him with younger boys and added to his feeling of inferiority. This was strengthened by overprotection from the mother who limited his physical activities, fearing the development of angina pectoris. Previously, the mother had refrained from carrying out instructions for tutoring as she considered that it would be too hard on him physically.

Socially he was maladjusted. His feeling of inadequacy prevented his leading through force of personality. He refused to boss. Thus he was solitary in his reactions. Through his intellectual, physical and social difficulties, he developed a feeling of inferiority without establishing an adequate defense mechanism. With

an emotional carry-over from the other fields he became a daydreamer, receiving no real satisfaction even in his mechanical ability.

Treatment consisted in endeavoring to remove the feeling of inferiority through building up self-confidence. He was reassured as to his results in mental tests, his normal mentality and his perfect result in the Stenquist mechanical test; he was the first boy at the clinic with a perfect performance. Several methods were used to correct his reading disability. One of these was remedial teaching with McCall reading tests. His good results in these tests were used as additional spurs. The mother was also reassured as to his normal mentality and was urged to cooperate by giving encouragement. She finally has been able to render him much help in additional difficult situations that have arisen. Much credit is due to the school for his improvement, for they have cooperated, creating opportunities in which he could experience success rather than failure. With treatment his feeling of inferiority has lessened so that he has made his own satisfactory social adjustment. He has found pleasure in being a leader in a boy scout group, is planning on having a troop of his own and at present is the head of a scout study group although he is the youngest. He has completed the first year of high school with the exception of English. Previously he never read any book, magazine or newspaper, but now he thoroughly enjoys reading. He is working for a local automobile agency and is planning on taking his entrance examinations for the General Electric apprentice school, although he is still fearful of examinations. His adjustment is satisfactory. One does not feel, however, that he will be entirely free from difficulties in the future.

A Case of Cerebellar Agenesis with Interesting Roentgen Observations. Dr. J. C. Yaskin.

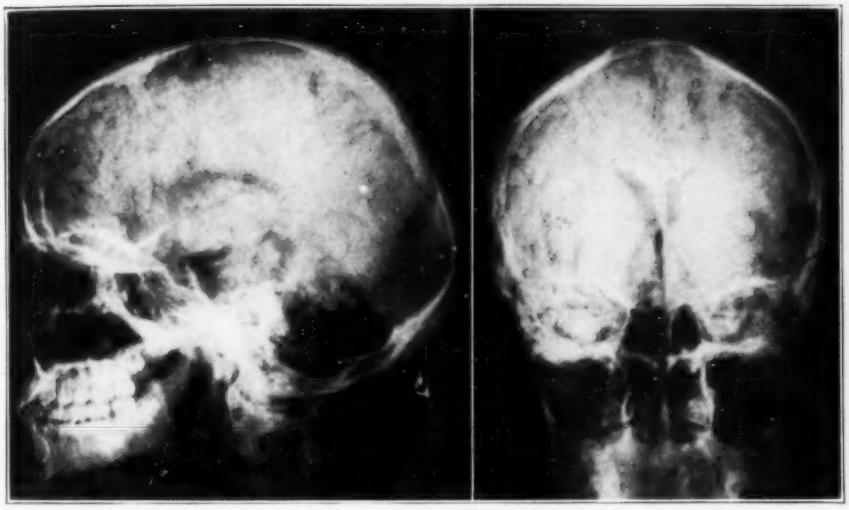
The principal reason for presenting this case is that a diagnosis of a rather unusual clinical entity was confirmed by an encephalogram. Also the evolution and course of the symptoms in this case of cerebellar deformity is unusual and raises the question as to whether it is a failure of development, with an abiotrophy, or a pathologic process occurring in early childhood, causing arrested development or degenerative changes in the cerebellum.

History.—L. D., a girl, aged 16, was admitted to the Graduate Hospital (Service of Dr. T. H. Weisenburg) complaining of inability to walk, nervousness and retarded progress at school. The family history is irrelevant. The patient is the second of three children; she was born at term by normal delivery. She had serious feeding difficulties until about 8 months, and did not talk or walk until about the age of 2 years. She gained control of the sphincters at about 2½. The mother does not recall that the child had any serious difficulties in walking until about the age of 5 when she suddenly fell and was unable to walk or use her hands because of weakness. This was diagnosed as chorea and she was kept in bed for several weeks. Ever since, she has had difficulty in walking and the use of her hands. She stumbles and falls easily, especially when hurried or going up and down the stairs. She can dress and feed herself, but always had trouble with writing. She entered school at 7½ years and, despite the disabilities, the teasing and the physical annoyances from the other children, managed to make good progress so that now she is in the second year of high school. Of late, however, the work has become more difficult, for she has difficulty in grasping the subjects, especially matters that require reasoning. Her speech, which has always been slow and deliberate, has become worse. She has noticed that the right hand and leg are becoming more clumsy. The mother states that she has become more irritable and difficult to get along with. Apart from these difficulties, the past medical history is unimportant.

Examination.—The results of a general physical examination were negative. The patient appeared well nourished and developed.

The patient maintains a silly grin and often laughs foolishly. She comprehends and executes commands readily. The cranial nerves show the following abnormalities: Overfulness of the veins in the left eyeground. Frequent horizontal

nystagmoid movements occur on looking either to the right or to the left, with the quick component to the side of deviation; there is no vertical nystagmus. The tongue is large and shows a coarse tremor on extension. All movements are carried out slowly but somewhat jerkily. When told to move faster, the patient says that she cannot do so. There is some weakness in both hands, more in the left than in the right, although the dynamometer reading is 32 in both. Although right-handed, she prefers to use the left hand. There is no appreciable disturbance of tonus in either upper extremity. The lower extremities are somewhat spastic, more on the right side. The biceps, triceps and abdominal reflexes are normally active; the patellar and ankle jerks are exaggerated, more on the right side; there is no Babinski sign or clonus on either side. The gait is with a wide base and with bending forward. The patient does not swing her arms, especially the right. In walking around the chair, she stumbles on clockwise and counterclockwise movements. She sways in the Romberg position and cannot stand on one leg, especially the right. She is totally unable to walk in a straight line, falling to one side



A B

Fig. 1.—Encephalograms in cerebellar agenesis, showing: *A*, the outline of the cerebellum with some atrophy in the frontal region and also at the vertex; *B*, filled lateral ventricles with some apparent disturbance in the contour of the cerebrum, especially at the vertex and in the left sylvian area.

or the other. She has a few choreiform twitchings of the hands when she makes voluntary movements such as taking off her stockings and shoes, etc., but not when at rest. There is a slight tremor of the outstretched hands. In the finger-to-nose test she develops a coarse tremor and often fails to strike the nose, especially with the right hand. In testing for diadokinesias, the left arm lags and swings through a wider circle than the right, both finally becoming dyssynergic. The patient tires easily; she can open and close her hands for only fifty-five seconds. She is particularly clumsy in movements requiring finer coordination of the hands, as was demonstrated by the handwriting. There was definite hypermetria in the heel-to-knee test on both sides, and there was ataxia on keeping the heel on the knee. Nowhere was there any disturbance of superficial or deep sensibility, of sense of position, vibration or stereognosis. Speech was slow and deliberate. The neurologic observations were those of dyssynergia of the trunk, extremities and speech.

Psychometric examination showed the patient to have an intelligence quotient of 73, the chronologic age being 16 years and 3 months while the mental age was 11 years and 8 months, and to belong in a borderline deficiency, with very dull intelligence, inferior in reasoning, comprehension, ability to see relationships and capacity for generalization.

Routine Laboratory Investigations.—Blood counts, blood chemistry examinations, the Wassermann test and spinal fluid studies all gave negative results. Roentgenograms of the skull were negative for evidence of increased intracranial pressure. Results of the Bárány tests were essentially negative.

Diagnosis.—A clinical diagnosis of cerebellar agenesis was made. An encephalogram made by Dr. Grant revealed the following interesting facts, as reported by Dr. Pfahler: "Encephalogram of this patient's skull shows an increased aerated space in the region of the cerebellum, more on the right side than on the left. It seems that even the outline of the convolutions of the cerebellum is shown" (figs. 1 and 2).

Comment.—The small size of the cerebellum, which strictly is not an agenesis, raises the question as to whether this is a congenital condition, a hypoplasia, an abiotrophy, or possibly some inflammatory process which commenced at the age of about 5 when the dyssynergic phenomena were first definitely observed. The cortical atrophy noted over the frontal poles and at the vertex, as well as in the left sylvian region, may explain the mental retardation and difficulties in speech as well as the spasticity. The marked involvement of the cerebellum as seen in figure 1, is, however, the most striking observation. The appearance of the symptoms more or less suddenly at the age of 5, and the tendency to progression rather than compensation would speak for an abiotrophy rather than a hypoplasia. The rather slow progression of the symptoms would probably indicate an abiotrophy rather than a degeneration secondary to an inflammatory or vascular process.

A Case of Primary Degeneration of the Pyramidal Tracts. Dr. J. C. Yaskin.

The literature on primary lateral sclerosis, first described by Erb and Charcot, has been considerably enriched by contributions by Minkowski, Strümpell, Dejerine and Sottas, Donnaggio, Friedman, Bichoff, Democh, Oppenheim, Mills and Spiller, (*Journal of Mental and Nervous Diseases,* July, 1903) and others. The evolution and course of this disease is eminently chronic. There is usually a gradually oncoming spastic paresis of the lower extremities, usually more of one side than of the other. In the course of years the lower limb becomes markedly spastic, and the condition spreads to one or both upper extremities. Strümpell has described laryngeal spasm, and bulbar laughing and crying due to the extension of the process into the bulb. Spiller and Mills (*Bulletin University of Pennsylvania,* 1906) have described a unilateral type of the disease. The disease may last for many years and, according to Oppenheim (Lehrbuch der Nervenkrankheiten, Berlin, 1923, vol. 1, p. 230), may even cease to progress. Pathologically, there is a primary isolated sclerosis of lateral tracts from the lumbar region to the internal capsule. The condition is difficult to differentiate, at least in the early stages, from amyotrophic lateral sclerosis, from compression of the cord by various causes, from the various types of myelitis and from multiple sclerosis.

This case is of interest because of its long duration, with involvement of the right lower extremity fourteen years ago, a long period of quiescence with only slight disability, until about three months ago, when implication of the left leg and right hand appeared.

History.—F. C., aged 42, a carpenter, was admitted to the Graduate Hospital, service of Dr. T. H. Weisenburg, on Dec. 11, 1928, complaining of weakness of the right leg and pain in the back. The family and past medical histories were of no etiologic value; the patient denied venereal infection, and never drank or smoked to excess. He first noticed weakness of the right leg fourteen years before. He went to the Methodist Hospital where a "nerve" was removed from

the calf of the right leg. The wound was about eight months in healing. The weakness of the leg persisted, but he was able to work until about six weeks before admission (November, 1928) when the right leg became much weaker; he also noticed, in addition, weakness of the left leg and right hand, and a dull aching pain in the lumbar region when he stood or walked for any length of time. There was no disturbance of sphincters or diminution of libido.

Examination.—A general physical examination gave negative results. The cranial nerves were normal. The right hand was distinctly weaker than the left, the former registering 85 and the latter 120 on the dynamometer (the patient is right-handed). There was wasting of the interosseal muscles, but none of the thenar or hypothenar areas of the right hand. There was no appreciable loss of power in the forearms or arms nor was there any disturbance of tonus. The biceps and triceps jerks were bilaterally exaggerated, much more on the right side. The Hoffman sign was negative. The abdominal and cremasteric reflexes were not obtained. Truncal movements revealed no weakness. Both lower extremities were spastic and weak, much more on the right side. The right thigh and leg were smaller than the left, the former measuring 18 and 11 inches (45.7 and 27.9 cm.), the latter 19 and 12 inches (48.2 and 30.5 cm.), respectively. The patellar and ankle jerks were bilaterally exaggerated, with a bilateral Babinski phenomenon and an ankle clonus on the right side. There was no disturbance of sensibility, deep or superficial, in any of the extremities, nor was there asynergia in any form.

Roentgen studies of the skull and spine were essentially normal. The blood count, blood chemistry, Wassermann reaction of the blood and observations on the cerebrospinal fluid were entirely normal. Functional gastric analysis revealed a normal hydrochloric acid curve. Special examinations excluded the existence of focal infections in the teeth, nasopharynx and genito-urinary tracts.

In the past two months there has been a further considerable loss of power in the right leg and to a lesser extent in the left leg and right arm.

DISCUSSION

DR. JOSEPH MCIVER: I once observed a case of supposed primary lateral sclerosis over a period of about ten or twelve years. The condition began about 1914, and until 1926 all symptoms were essentially those of disease of the pyramidal tract. The trouble began first in the right leg, later in the left leg, then in the right arm and last in the left arm. After twelve years the patient began to show muscular atrophy around the shoulder girdles. The muscles of the thigh and calf also began to waste away. It could no longer be regarded as a case of primary lateral sclerosis but was undoubtedly one of amyotrophic lateral sclerosis.

More recently, I observed a man over a period of three years, who had at first only symptoms of the pyramidal tract; at the end of this time, however, he began to show muscular wasting in the shoulder girdles. I have begun to wonder whether or not primary lateral sclerosis is a disease entity.

DR. MCCONNELL: There was another case of primary lateral sclerosis in the Philadelphia General Hospital which showed nothing at all until Dr. Lloyd discovered that the man had atrophy of the pectoralis major muscle on one side. When the patient died, I believe the diagnosis was amyotrophic lateral sclerosis.

In Dr. Yaskin's case, I did not hear anything about eyegrounds and abdominal reflexes. I think that the diagnosis of primary lateral sclerosis should be held up for a time.

DR. C. A. PATTEN: Does Dr. Yaskin consider the case of cerebellar agenesis congenital or something that happened at birth?

DR. JOSEPH C. YASKIN: In reply to Dr. McConnell, there was nothing abnormal in the eyegrounds; both fields and fundi were normal. All laboratory studies gave negative results. Neither abdominal nor cremasteric reflexes could be obtained. There were no signs of atrophy. The right hand was weaker, but there was no evidence of trophic disturbance.

Regarding Dr. Patten's question as to whether or not it was congenital, I do not know. This child was doing fairly well until 5 years of age, when she suddenly fell. After that she was unable to use the arms and legs for several weeks. Since 5 years of age, she has been having these phenomena and has been getting progressively worse. It occurred to me that if it were a congenital condition, she would have shown it much earlier. I think something happened at the age of 5, an activation of some congenital weakness or loss, or some inflammatory or vascular process that has progressed slowly ever since.

CEREBELLAR AGENESIS: PRELIMINARY REPORT OF AN EXTREME CASE. DR. WALTER FREEMAN.

Agenesis of the cerebellum and its dependencies has been reported a considerable number of times, but has rarely been as complete as in the specimen presented.

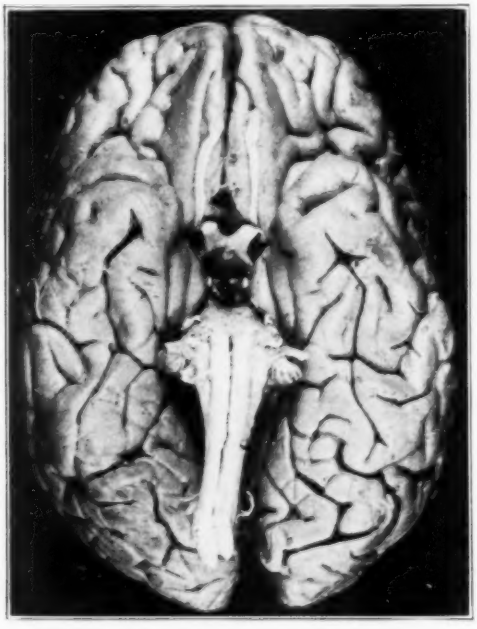


Fig. 1.—Extreme cerebellar agenesis, with absence of the pons and olivary bodies.

This case deserves to be classed with the famous ones of Combette (Absence complète du cervelet, *Bull. Soc. anat. de Paris,* 1831, p. 148; second ed., Paris, 1846), Flechsig (Plan des menschlichen Gehirns, Leipzig, Veit, 1883, pp. vii, 18 and 25), Sternberg (*Verhandl. d. deutsch. path. Gesellsch.* **15**:353, 1912) and Anton and Zingerle (*Arch. f. Psychiat.* **54**:8, 1914). The patient presented relatively little incoordination, a phenomenon noted in other cases of complete primary cerebellar agenesis, and explained by Anton on the basis of compensatory activity by the more recently acquired neokinetic system. Indeed, severe incoordination in this patient seemed to develop about the time that arteriosclerotic changes impaired the circulation of the brain and led to multiple infarcts in the parietal lobe.

History.—O. T., a colored man, aged about 72, was admitted to St. Elizabeth's Hospital in March, 1926 and died in October, 1928. On admission he was stooped and tremulous, could walk only with assistance, was markedly incoordinate in his

movements and could not talk intelligibly. The history from a brother indicated that the patient had always been somewhat subnormal mentally and had never gone to school, but that he had walked and talked at about the usual time, had supported himself since adolescence by doing odd jobs of gardening, repairing, trucking, etc., had been able to handle his money and was reliable. He had never married, but had lived with his brother for many years. The brother stated specifically that although the patient's left leg was shorter than the right, he could run about and play the games of childhood in a normal manner.

In 1925, the patient showed increased bending to the left and forward, and developed a tendency to fall. He was picked up on the streets in a confused condition and was eventually brought to St. Elizabeth's Hospital.

Examination.—Memory was defective. The patient could not count beyond ten, and expressed vague delusions about talking with God. Physically, he was fairly well nourished, talking in a jerky, slurring manner; he walked with the trunk bent far forward and to the left and frequently fell to the floor when not supported. The pupils reacted rather sluggishly to light. Both deep and superficial reflexes were equal and active on the two sides, and no pathologic signs were elicited. There were coarse intention tremors of all four limbs, and "athetoid" movements of the hands. Aside from impaired resonance with harsh breath sounds at the apexes, and considerable underdevelopment of the left leg, the physical examination gave negative results. The Wassermann reaction was negative.

Course.—During his stay in the ward the patient spent most of his time in bed, but was occasionally allowed to sit up in a chair. Sometimes he lurched about the ward, clapping his hands, turning somersaults and trying to stand on his head. On account of incoordination he had to be spoon-fed. Death resulted from tuberculosis.

Necropsy.—Necropsy disclosed tuberculosis of the lungs and lymph nodes, with moderate emaciation. On removing the calvarium the dura was found relaxed, the pia thin, and the blood vessels sclerotic. In the left parietal region were numerous brownish puckerings in the cortex. The tentorium was unusually small, but presented a normal incisura. The posterior fossa was much constricted generally, with an abrupt clivus.

The cerebellum was represented by two nubbins of convoluted form situated in the region of the flocculi, that on the left measuring 8 by 7 by 5 mm. and that on the right 8 by 6 by 5 mm. The roof of the fourth ventricle was composed of a peaked translucent membrane extending from the velum interpositum to the calamus scriptorius, and attached at the lateral borders of the fourth ventricle. It contained choroid plexus. The floor of the ventricle was unusually broad and showed no striae acusticae, although some other normal eminences could be identified. Two fusiform bodies situated laterally probably represented the cerebellar nuclei. The posterior corpus quadrigeminum appeared to be absent on the right side. The aqueduct was wider than normal. On the ventral aspect of the specimen the pons was represented by a thin sheet of tissue barely concealing the underlying pyramidal tracts. The cerebellar peduncles were rudimentary. In place of the normal olivary prominence there was a deep furrow. The pyramids appeared proportionately, and possibly absolutely, large.

Comment.—Patients with severe cerebellar agenesis seldom live long. Usually there are other defects, such as spina bifida and hydrocephalus. Mental deficiency is common. A detailed anatomic study of this case is being undertaken, but I believe that the gross specimen should be placed on record in this preliminary report.

Book Reviews

TUMORS ARISING FROM THE BLOOD VESSELS OF THE BRAIN. By HARVEY CUSHING and PERCIVAL BAILEY. Price, $7.50. Pp. 220, with 159 illustrations. Springfield, Ill.: Charles C. Thomas.

The lead is again taken by the Cushing clinic in the discussion of a group of tumors of the nervous system which are composed either of fully formed blood vessels or of the cellular elements of the blood vessels. The former, discussion of which comprises one half of the book, are really not tumors in the strictest sense of the word. They are the angiomas which are capillary, venous or arterial, and are either considered as congenital lesions or have a vascular malformation as their basis. Explanation is made and examples are given as to how they exert pressure and therefore are to be considered in the same domain as tumors.

Of the entire group of tumors in the Cushing collection, consisting of 1,522 tumors of all kinds, only 29, or about 2 per cent, are in association with the blood vessels. Of these sixteen are in the first group of vascular malformations and only one is considered a telangiectasis; six, angioma venosum, all of which were diagnosed only by inspection, and nine, angioma arteriale, of which eight were diagnosed by inspection and bruit. It is an interesting fact, which every pathologist can verify, that the histologic differentiation of these three groups can be exceedingly difficult, and gross examination may at times be a better criterion in the differential diagnosis. Of this the authors, of course, are aware and state rather clearly that the microscope can be actually misleading, as shown by the early interpretation of some of the lesions which were at one time or another reported as tumors of different kinds.

The case of telangiectasis is of more than ordinary interest in that it occurred in a patient, who was considered as having a case of hysteria, in whom an exploratory operation did not reveal the "tumor" and who for eight years after the operation was able to resume the work of teaching. She died suddenly and an autopsy showed the lesion in the upper part of the pons.

The venous angiomas are divided into three groups: the simple varices, the serpentine and the racemose or circoid. In many of these the symptoms were those of tumors of the brain, and only at operation was the true nature of the "growth" discovered. The characteristic of this venous group is that the "tumor" does not pulsate, in contrast to the following group of arterial tumors in which pulsation occurs. As one reads the histories of case after case in this group no surprise is felt that operations were done. At first, the tendency of the surgeon was to attempt removal or at least ligation, in some cases with dire results. In one case in which the lesion was located over the motor area and removal was attempted, the result was so bad that a more cautious attitude was assumed in the following cases in many of which no attempt was made to treat the lesion by ligation or otherwise. In many of the patients, roentgen treatments were given, in some with beneficial results. It is of interest from the clinical aspect to know that because of their superficial character jacksonian epilepsy was present in three of the five cases. One should keep in mind that in many of these patients a nevus of the face may be the sign in diagnosis, as in a case of Spiller's in which an accurate diagnosis was made.

In some cases, the arterial angiomas showed an intracranial bruit, although this was absent in others. Clinically, it may be said that "when an audible intracranial bruit is coupled with increased extracranial vascularity it is the most likely element on which a correct clinical diagnosis may be based." Cushing comments on the fact that auscultation of the skull is the one routine neurologic examination which is most often neglected.

A bibliography is appended to this part of the subject, with 160 references.

The second part of the book, written in the same case history manner, considers lesions which are unmistakably neoplastic and which are composed of the same elements that enter into the development of the primordial blood channels. All of these tumors are classed under the name of hemangioblastomas. The authors believe that the angioblastic tumors prove to be more common in, if not actually confined to, the cerebellum, in contrast to the angiomas which occur in the cerebrum. Many of these cases were formerly considered and even reported as vascular gliomas, which because of advances in staining methods have been proved not to belong to the glioma group. Many of the cases fit into the group described by Lindau, and since called Lindau's disease, in which vascular lesions of the retina were associated. The authors have had examinations of the eyegrounds made in some of their old cases with both positive and negative observations.

It must be realized that angiomatous tumors of the cerebellum give the same sort of symptoms as other tumors and can be diagnosed only by operation. The authors state that in none of the eleven cerebellar cases reported was the true nature of the lesion suspected, although in one there was an angioma of the retina which would have served to make the diagnosis had it been recognized and its significance appreciated. Hippel's angiomatosis retinae was not known until attention was directed to it by Lindau's report in 1912.

This book, written in case history style, is admirable, not only for those interested only in the clinical pictures but also for pathologists. The histologic divisions are simple and sufficient. A book of this sort is a definite step forward in the consideration of a group of lesions, which, while not common, are of importance for the neurologist, neurosurgeon and pathologist. The illustrations are numerous and of good quality. The publishers are to be congratulated for their part of the work; it is most excellently done. This book should be in the possession of all who are interested in the clinical and pathologic aspects of the problems of tumors of the brain.

L'HYGIÈNE DE L'ATTENTION PAR LA MÉTHODE D'AUTORÉGULATION CONSCIENTE. By R. RUIZ ARNAU, M.D. Paper. Price, 25 francs. Pp. 284, with 19 illustrations. Paris: Gaston Doin, 1928.

In this book the author represents the results of studies in the hygiene of vision, previously published in book form (El Uso Natural de la Vision, New York, D. Appleton & Company, 1924) with amplifications that extend the application of the principles involved in the general hygiene of attention. The book is divided into three parts. Part I deals with the general nature of attention and follows closely the lines laid down by Ribot. By the use of the tachorthoscope and other methods it is demonstrated that voluntary or artificial attention, like spontaneous attention, is an oscillatory activity requiring alternate contractions and relaxations for its normal performance. Efforts to maintain steady fixation of attention defeat its purpose and result in diminished acuity of perception as the result of fatigue. Continued practice of such voluntary muscular contractions results in the occurrence of spasms that involve both striated and unstriated muscle and give rise to many varieties of clinical disorder of function, which may be accompanied eventually by structural changes. The prevention of these conditions can be accomplished by the acquisition of habits of oscillatory fixation, which means learning to make use of relaxation in accord with the rhythm of spontaneous or natural attention—that of the pulse rate or some factor of it. Such acquired oscillatory control is spoken of as conscious autoregulation.

In part II the author discusses the application of this discipline in relation to the general prophylaxis of nervous states, and in particular to: the myopia of school children, with reports of results secured with large groups of children both in the United States and in Europe; the broad field of asthenopia, with which are included migraine and seasickness, and diseases of the vascular system.

Part III is devoted to a detailed exposition of the various technics available for learning habits of autoregulation, not only visual but also auditory and

kinesthetic. Stress is laid on the fact that these exercises in no way interfere with any occupation and do not cause fatigue.

The material presented deserves the most serious consideration of all who are interested in educational methods as well as of physicians and others engaged in the care and treatment of patients suffering from functional nervous disorders. This means every physician, as such disorders constitute a large proportion of all medical practice. The method is not presented as a panacea, but is an unquestionable contribution to the large and growing recognition of the importance of relaxations in the realm of mental hygiene.

LA PSYCHOANALYSE DES NÉVROSES ET DES PSYCHOSES (SES APPLICATIONS MÉDICALES ET EXTRA-MÉDICALES). By E. RÉGIS and A. HESNARD. Third edition. Price, 25 francs. Pp. 440. Paris: Librairie Felix Alcan.

Régis, as the most didactic of the French psychiatrists of the transition period that held out against the kraepelinian invasion, was the first to present an evaluation of psychoanalysis, with his pupil Hesnard, in 1914. Régis remained a critical reporter. Hesnard was converted, and is today one of the protagonists of the freudian wing of French psychiatry. The book, in this third edition, renders the text of the master, but is at the same time recast and brought up to date with the help of additional discussions. The appointment of the internist-neurologist Claude as successor of Dupré to the leading psychiatric clinic of France opened the door to Bleuler's and Freud's views with a background of biologic-physiologic ambitions, presented in the ARCHIVES (**13**:729 [June] 1925); under this eclecticism the freudian school added welcome material of progressiveness. The book, therefore, is to some extent a picture of what was bound to come after the premature death of Régis. Ribot and Janet remained practically without pupil or co-worker of note. Dumas and Piéron remained on largely experimental ground, and the classic clinical psychiatry failed to make the transition to a dynamic point of view so significant in the psychiatry of this century, and just as Rome failed to develop a religion of its Roman lights and borrowed the cult of the lowly, so France is coming to borrow the psychopathology of Freud, cult and all.

The theory of psychoanalysis is presented in a chapter on the history of its development, one on the dynamic psychology and the unconscious, the censorship, and super-ego, Freud's schemata and the complexes and their affective significance. There follows the sex theory of Freud, then the technic of analysis and the associations and lapses of everyday life. The second half of the book deals with the application of psychoanalysis in psychology, religion, art and literature, philosophy and pedagogy, and in the treatment for the neuroses and psychoses (dementia praecox, paranoia and the manic-depressive psychoses), the therapeutic rôle, and finally the critique giving the original statement of Régis and the corrections from Hesnard's present experience. A selected bibliography closes the book.

The aim to show how the new facts and theories can and must be incorporated in the "classic" French neuropsychiatry is lucidly brought forth. As a supplement to the new French journal for psychoanalysis, the book offers a good orientation of the trend of psychoanalysis in France.

AN DEN GRENZEN DER PSYCHIATRIE. By OSWALD BUMKE. Paper. Price, 4.20 marks. Pp. 86. Berlin: Julius Springer, 1929.

"On the Borders of Psychiatry" consists of four bright but intelligently conservative essays on telekinesis, hysteria and stupidity, psychopathology and art, culture and degeneracy and the present day currents in psychology.

The first essay is a wholesome, half humorous, half serious discussion of a case of "telekinesis," bearing out the catchwords of the title, cleverly put and free from any offensive dogmatism or unnecessary preaching ex cathedra: a well told story of how a slightly more than physiologically stupid servant girl thoroughly deceived a not altogether small circle of people and stirred up the press throughout Germany.

The second one contains a wholesome evaluation of the loose identification of art and talent and genius and pathology. The author looks for less perversion and less morbidness in the coming epoch.

In the third essay, Bumke meets the pessimism concerning culture and degeneracy in a sane and well balanced manner. He is finally most concerned about the ill considered advocacy of license as to abortion, the reduction of fecundity among the intelligent and active and the predominance of the sick and the stupid elements.

The fourth essay is devoted to the basic facts of psychology in contrast to the groping for absolutes and essences and the philosophic unconscious and the like. The year 1874 brought the elementalism of Wernicke and that of Wundt. Their physicalism and elementalism were shaken up in 1894 by two movements, Dilthey's descriptive psychology and Breuer and Freud's first steps toward psychoanalysis, both working with personality function, with facts accessible from many angles — an interesting development after the Moebius outcry of the hopelessness of all psychology.

In these days of futuristic literature it is pleasant to meet Bumke's combination of sobriety and brightness of vision and exposition.

RECENT ADVANCES IN NEUROLOGY. By W. RUSSELL BRAIN and E. B. STRAUSS, London. Price, $3.50. Pp. 412. Philadelphia: P. Blakiston's Son & Company, 1929.

This volume presents a résumé of recent advances in neurology. In a small book of this kind it would have been impossible for the authors to have taken up every phase of such progress. As it is they have made an excellent selection. The subjects by chapters are as follows: The Circulation of the Cerebrospinal Fluid; Diagnosis of Spinal Block; Intracranial Tumour; Path of the Visual Fibres. Visual Defects with Special Reference to Intracranial Tumours; The Treatment of Increased Intracranial Pressure by Means of Hypertonic Solutions; The Regulation of the Cerebral Circulation; Intracranial Aneurysm; Posture and Tonus; Paraplegia and Hemiplegia; The Cerebellum; Extrapyramidal Syndromes; The Pituitary and the Hypothalamus; Conditioned Reflexes; Sleep, Normal and Pathological; Sensation; Neurotropic Viruses; Epidemic Encephalitis; Miscellaneous Neurological "Diseases" of Recent Description; The Intravertebral Treatment of Diseases of the Central Nervous System; Miscellaneous Therapeutic Advances; X-Ray Treatment of Diseases of the Nervous System, and Cerebrospinal Fluid "Pictures" in Various Common Neurological Conditions.

It would be easy to criticize the manner of presentation. Certain points of view were adopted, while others that the reviewer might consider of even greater value, were arbitrarily rejected. In a controversial subject, however, perhaps one point of view is as good as another, and after all the authors must be given the privilage of selection and presentation as they see fit. On the whole, the subject is impartially presented and is a distinct addition to those who like to read their neurology in such form.

MODERN PROBLEMS IN NEUROLOGY. By S. A. KINNIER WILSON. Price, $6. Pp. 364. New York: William Wood & Company, 1929.

This volume contains a series of papers which have appeared during the last few years in various journals, mostly British. One article has appeared in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. They are therefore familiar to neurologists. The subjects are as follows: The Epilepsies; Epileptic Variants; Inhibitory Epilepsy; The Psychical Components of Temporal (Uncinate) Epilepsy; The Narcolepsies; The Old Motor System and the New; Disorders of Motility and Muscle Tone — The Voluntary Motor System in Striatal Disease; Disorders of Muscle Tone in Striatal Disease; Involuntary Movements and Their Pathogenesis: Chorea and Athetosis; Involuntary Movements and Their Pathogenesis: Tremor; General Survey of Striatal Motor Function; Pathological Laughing and

Crying; Dysaethesiae and Their Neural Correlates, and The Argyll Robertson Pupil. The author has brought these subjects up to date, that is, he has added a consideration of the literature but in no way has modified his original point of view.

The publication of these papers in one volume is of distinct service, for it brings to the attention of neurologists a broad physiologic conception of some of the outstanding problems in neurology. It is a credit to the author and to British neurology.

DISEASES OF THE NERVOUS SYSTEM. By SMITH ELY JELLIFFE, M.D., PH.D., and WILLIAM A. WHITE, M.D. Fifth edition. Price, $9.50. Pp. 1141, with 476 engravings and 13 plates. Philadelphia: Lea & Febiger.

Any textbook which has the distinction of running to the fifth edition must necessarily have been approved by the medical profession at large. The present volume, while it has been revised, is along the lines of previous editions. Additions have been made here and there, for advantage has been taken of the recent literature.

Obviously any work bears the stamp of the scientific trend of the authors; that they are chiefly interested in vegetative visceral neurology becomes at once apparent, for the part of the book which deals with this intricate subject receives more attention, and deservedly so, than in any other textbook with which the reviewer is familiar. The same is true regarding the endocrinopathies.

As is to be expected, the psychoneuroses and psychoses have a psychoanalytic trend. The part of the book which deals with organic neurology is adequately handled, but not on a par with visceral neurology.

SPINAL ANESTHESIA (SUBARACHNOID RADICULAR CONDUCTION BLOCK). Principles and Technique. By CHARLES H. EVANS, M.D. Price, $5.50. Pp. 203. New York: Paul B. Hoeber, Inc., 1929.

Spinal anesthesia is receiving an increasing amount of attention from the medical profession and deservedly so. The technic for administration has become much more refined so that, in the hands of those who know how to apply it, it is in many respects the anesthesia of choice. The book gives a clear exposition of this procedure. It is at once obvious that spinal anesthesia should not be used by one who is not familiar with all the pitfalls of the process, and that a thorough familiarization of all its dangers is necessary before it should be used. The book is exceedingly well illustrated and thoroughly done.

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